US 20160312307A1

(19) **United States**

(12) **Patent Application Publication** (10) **Pub. No.: US 2016/0312307 A1**

KENNEDY et al. (43) **Pub. Date: Oct. 27, 2016**

(54) **METHODS AND COMPOSITIONS OF MOLECULAR PROFILING FOR DISEASE DIAGNOSTICS**

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(21) Appl. No.: **15/164,230**

(22) Filed: **May 25, 2016**

Related U.S. Application Data

(63) Continuation of application No. 13/589,022, filed on Aug. 17, 2012, which is a continuation of application No. 12/592,065, filed on Nov. 17, 2009, now Pat. No. 8,541,170.

(60) Provisional application No. 61/199,585, filed on Nov. 17, 2008, provisional application No. 61/270,812, filed on Jul. 13, 2009.

Publication Classification

(51) **Int. Cl.**

C12Q 1/68 (2006.01)

G06F 19/20 (2006.01)

(52) **U.S. Cl.**

CPC ***C12Q 1/6886*** (2013.01); ***G06F 19/20*** (2013.01); *C12Q 2600/158* (2013.01); *C12Q 2600/112* (2013.01); *C12Q 2600/178* (2013.01)

(57) **ABSTRACT**

The present invention relates to compositions, kits, and methods for molecular profiling and cancer diagnostics, including but not limited to gene expression product markers, alternative exon usage markers, and DNA polymorphisms associated with cancer. In particular, the present invention provides molecular profiles associated with thyroid cancer, methods of determining molecular profiles, and methods of analyzing results to provide a diagnosis.

Input CEL File	Pathology
151329HUEX1A11.CEL	Benign
151345HUEX1A11.CEL	Benign
151326HUEX1A11.CEL	Benign
151380HUEX1A11.CEL	Benign
151289HUEX1A11.CEL	Benign
151338HUEX1A11.CEL	Benign
151315HUEX1A11.CEL	Benign
151306HUEX1A11.CEL	Benign
151316HUEX1A11.CEL	Benign
151276HUEX1A11.CEL	Benign
151305HUEX1A11.CEL	Benign
151330HUEX1A11.CEL	Benign
151336HUEX1A11.CEL	Benign
151275HUEX1A11.CEL	Benign
151309HUEX1A11.CEL	Benign
151284HUEX1A11.CEL	Benign
151295HUEX1A11.CEL	Benign
151279HUEX1A11.CEL	Benign
151293HUEX1A11.CEL	Benign
151359HUEX1A11.CEL	Benign
151325HUEX1A11.CEL	Benign
151283HUEX1A11.CEL	Benign
151361HUEX1A11.CEL	Benign
151294HUEX1A11.CEL	Benign
151373HUEX1A11.CEL	Benign
151364HUEX1A11.CEL	Benign
151308HUEX1A11.CEL	Benign
151291HUEX1A11.CEL	Benign
151285HUEX1A11.CEL	Benign
151363HUEX1A11.CEL	Malignant
151347HUEX1A11.CEL	Malignant

Figure 1

151346HUEX1A11.CEL	Malignant
151288HUEX1A11.CEL	Malignant
151340HUEX1A11.CEL	Malignant
151334HUEX1A11.CEL	Malignant
151300HUEX1A11.CEL	Malignant
151323HUEX1A11.CEL	Malignant
151319HUEX1A11.CEL	Malignant
151358HUEX1A11.CEL	Malignant
151365HUEX1A11.CEL	Malignant
151348HUEX1A11.CEL	Malignant
151320HUEX1A11.CEL	Malignant
151278HUEX1A11.CEL	Malignant
151304HUEX1A11.CEL	Malignant
151341HUEX1A11.CEL	Malignant
151281HUEX1A11.CEL	Malignant
151321HUEX1A11.CEL	Malignant
151339HUEX1A11.CEL	Malignant
151277HUEX1A11.CEL	Malignant
151286HUEX1A11.CEL	Malignant
151362HUEX1A11.CEL	Malignant
151382huex1a12.CEL	Malignant
151379HUEX1A11.CEL	Malignant
151376HUEX1A11.CEL	Malignant
151318HUEX1A11.CEL	Malignant
151352HUEX1A11.CEL	Malignant
151384HUEX1A11.CEL	Malignant
151354HUEX1A11.CEL	Malignant
151353HUEX1A11.CEL	Malignant
151344HUEX1A11.CEL	Malignant
151368HUEX1A11.CEL	Malignant
151324HUEX1A11.CEL	Malignant
151350HUEX1A11.CEL	Malignant
151317HUEX1A11.CEL	Malignant

Figure 1 Continued

151375HUEX1A11.CEL	Malignant
151367HUEX1A11.CEL	Malignant
151311HUEX1A11.CEL	Normal
151327HUEX1A11.CEL	Normal
151298HUEX1A11.CEL	Normal
151299HUEX1A11.CEL	Normal
151310HUEX1A11.CEL	Normal
151385HUEX1A11.CEL	Normal
151349HUEX1A11.CEL	Normal
151301HUEX1A11.CEL	Normal
151351HUEX1A11.CEL	Normal

Figure 1 Continued

Gene	DE p-value	FDR DE p-value	Fold-change Malignant/ Benign	Fold-change Malignant/ Normal	Fold-change Benign/ Normal
MYOC	6.40E-13	9.53E-09	-1.06	-2.45	-2.32
GPC3	5.31E-12	3.96E-08	-1.08	-2.23	-2.07
PLA2R1	3.11E-11	9.27E-08	-1.93	-3.36	-1.74
LMOD1	5.16E-11	1.10E-07	-1.17	-1.92	-1.65
MYEF2	6.15E-11	1.14E-07	1.69	2.42	1.43
LRP1B	1.74E-09	2.60E-06	-1.93	-2.42	-1.25
MPPED2	2.80E-09	3.47E-06	-2.05	-2.32	-1.13
GPM6A	3.32E-09	3.80E-06	-1.62	-2.87	-1.78
TBC1D4	8.68E-09	8.63E-06	-1.56	-2.01	-1.29
STK32A	9.74E-09	9.07E-06	2.54	3.26	1.29
KHDRBS2	1.12E-08	9.85E-06	-2.03	-2.63	-1.30
FN1	1.24E-08	1.02E-05	3.96	5.84	1.47
FLJ22655	1.28E-08	1.00E-05	-1.07	-1.86	-1.73
KIT	1.51E-08	1.12E-05	-1.88	-2.10	-1.12
MATN2	2.03E-08	1.26E-05	-1.91	-3.12	-1.63
C9orf58	2.19E-08	1.31E-05	-1.29	-1.90	-1.47
ChGn	2.56E-08	1.41E-05	-2.27	-2.99	-1.32
ANGPTL1	3.53E-08	1.88E-05	-1.44	-2.00	-1.39
FABP4	4.88E-08	2.42E-05	-3.31	-5.39	-1.63
SIPA1L2	8.59E-08	4.13E-05	1.56	1.92	1.23
XPR1	9.26E-08	4.31E-05	1.53	2.09	1.36
TBX22	9.39E-08	4.24E-05	-1.61	-2.43	-1.51
P4HA2	1.05E-07	4.48E-05	1.69	2.10	1.25
TPO	1.45E-07	5.83E-05	-3.18	-4.29	-1.35
TSC22D1	1.61E-07	6.31E-05	1.89	1.37	-1.38
JUN	1.77E-07	6.59E-05	-1.65	-3.06	-1.85
DPT	1.83E-07	6.67E-05	-1.69	-4.76	-2.81
GALNT7	2.59E-07	8.40E-05	1.82	2.08	1.14
SLC26A4	2.80E-07	8.70E-05	-3.22	-4.27	-1.33
ADH1B	2.91E-07	8.84E-05	-1.36	-3.48	-2.56
NRCAM	4.32E-07	1.15E-04	1.80	3.16	1.76

Figure 2

GABRB2	4.40E-07	1.15E-04	2.45	2.60	1.06
DPP6	5.04E-07	1.23E-04	-1.53	-2.45	-1.60
MAFB	6.56E-07	1.50E-04	-1.45	-1.87	-1.29
SDC4	6.85E-07	1.55E-04	2.13	1.95	-1.09
FOSB	1.03E-06	2.10E-04	-1.24	-1.93	-1.56
EPHA3	1.06E-06	2.13E-04	-1.20	-2.11	-1.75
ARHGAP24	1.17E-06	2.27E-04	-1.76	-2.04	-1.16
C11orf74	1.39E-06	2.49E-04	-1.73	-2.50	-1.45
PI16	1.90E-06	3.22E-04	-1.14	-2.08	-1.82
CP	1.94E-06	3.22E-04	-2.48	-3.28	-1.32
LRP2	2.03E-06	3.29E-04	-2.14	-2.07	1.03
LIPH	2.37E-06	3.64E-04	1.80	2.22	1.23
RAB23	2.72E-06	4.06E-04	-1.42	-2.17	-1.53
TUSC3	2.79E-06	4.11E-04	1.94	2.43	1.26
GLT8D2	3.34E-06	4.61E-04	-1.54	-3.07	-1.99
TRPC5	4.05E-06	5.29E-04	1.81	1.91	1.06
TNIK	4.10E-06	5.27E-04	1.34	1.99	1.48
SCEL	4.44E-06	5.56E-04	1.87	2.05	1.09
TNFRSF11B	4.54E-06	5.64E-04	-1.73	-2.41	-1.39
CAMK2N1	5.48E-06	6.48E-04	2.92	2.23	-1.31
LGALS3	5.85E-06	6.81E-04	1.95	1.81	-1.08
SCG5	6.09E-06	7.03E-04	3.16	2.81	-1.13
DPP4	6.98E-06	7.70E-04	2.55	3.30	1.29
OGN	6.99E-06	7.65E-04	-1.21	-2.05	-1.69
PGCP	7.53E-06	8.07E-04	-1.47	-1.99	-1.35
NRIP1	7.92E-06	8.37E-04	1.73	1.86	1.08
SDC2	9.39E-06	9.39E-04	-1.67	-2.64	-1.58
CD36	1.08E-05	1.04E-03	-2.03	-1.95	1.04
CRABP1	1.14E-05	1.09E-03	-2.65	-6.83	-2.58
EFEMP1	1.17E-05	1.10E-03	-1.56	-2.43	-1.56
MFAP4	1.30E-05	1.18E-03	-1.05	-1.91	-1.81
ITGA2	1.36E-05	1.23E-03	1.73	2.20	1.27
DUSP1	1.56E-05	1.36E-03	-1.33	-2.28	-1.72

Figure 2 Continued

EGR1	1.78E-05	1.51E-03	-1.30	-2.55	-1.97
EGR2	2.03E-05	1.66E-03	-1.75	-3.38	-1.93
SORBS2	2.15E-05	1.69E-03	-1.67	-2.06	-1.23
MET	2.21E-05	1.72E-03	2.09	2.32	1.11
CLDN16	2.27E-05	1.74E-03	2.48	3.55	1.44
PSD3	2.76E-05	2.02E-03	1.76	2.13	1.21
RABL3	3.17E-05	2.21E-03	-1.97	-1.94	1.02
APOD	3.17E-05	2.20E-03	1.05	-3.54	-3.70
PCOLCE2	3.74E-05	2.52E-03	-1.32	-2.76	-2.10
ITM2A	3.89E-05	2.57E-03	-1.56	-1.99	-1.28
ETV5	3.91E-05	2.56E-03	1.56	1.96	1.26
PROS1	4.50E-05	2.79E-03	1.64	1.95	1.19
HBB	4.52E-05	2.79E-03	-1.65	-5.19	-3.15
CYR61	4.63E-05	2.83E-03	-1.92	-2.58	-1.35
NFE2L3	4.65E-05	2.83E-03	1.44	2.01	1.39
FOS	4.74E-05	2.86E-03	-1.28	-2.11	-1.65
DLG2	5.87E-05	3.32E-03	-1.44	-2.02	-1.40
PKHD1L1	5.91E-05	3.31E-03	-2.55	-3.84	-1.50
C9orf61	6.09E-05	3.39E-03	-1.81	-2.04	-1.12
AMIGO2	7.93E-05	4.21E-03	1.78	2.05	1.15
ALDH1A1	9.36E-05	4.74E-03	-1.81	-2.15	-1.19
PSD3	1.06E-04	5.13E-03	1.43	1.91	1.33
LIFR	1.10E-04	5.23E-03	-1.77	-2.34	-1.32
C7orf24	1.30E-04	5.88E-03	1.58	1.96	1.24
RAG2	1.37E-04	6.12E-03	-1.86	-1.55	1.20
S100A2	1.45E-04	6.41E-03	2.42	1.39	-1.74
WDR72	1.47E-04	6.43E-03	-1.92	-2.51	-1.31
MT1G	1.53E-04	6.55E-03	-2.49	-3.07	-1.23
DCN	1.56E-04	6.65E-03	-1.06	-5.24	-4.95
ZNF804B	1.62E-04	6.85E-03	-1.20	-2.21	-1.85
CTGF	1.64E-04	6.86E-03	-1.92	-2.83	-1.48
RHOBTB3	1.65E-04	6.90E-03	1.68	1.99	1.18
DNAJB4	1.65E-04	6.86E-03	-1.31	-2.13	-1.62

Figure 2 Continued

SERPINA1	1.65E-04	6.87E-03	2.89	3.08	1.07
QPCT	1.68E-04	6.90E-03	2.01	2.09	1.04
TMEM171	2.46E-04	9.30E-03	-1.51	-2.92	-1.93

Figure 2 Continued

Gene	Alt. Exon p-value	Alt. Exon FDR p-value
TPO	0.00E+00	0.00E+00
DPP6	0.00E+00	0.00E+00
LRP1B	0.00E+00	0.00E+00
KIT	0.00E+00	0.00E+00
CD36	0.00E+00	0.00E+00
RHOBTB3	0.00E+00	0.00E+00
CTSB	0.00E+00	0.00E+00
SLC4A4	0.00E+00	0.00E+00
ANKS1B	0.00E+00	0.00E+00
MDM2	0.00E+00	0.00E+00
ABCA8	0.00E+00	0.00E+00
CDH6	0.00E+00	0.00E+00
CENPJ	0.00E+00	0.00E+00
ABCA1	0.00E+00	0.00E+00
DIO2	0.00E+00	0.00E+00
PON2	0.00E+00	0.00E+00
SLC20A1	0.00E+00	0.00E+00
FBXL20	0.00E+00	0.00E+00
PCNX	0.00E+00	0.00E+00
PGM2L1	0.00E+00	0.00E+00
RASGRP3	0.00E+00	0.00E+00
ZEB1	0.00E+00	0.00E+00
AAK1	0.00E+00	0.00E+00
AFAP1L2	0.00E+00	0.00E+00
C12orf63	0.00E+00	0.00E+00
DYX1C1	0.00E+00	0.00E+00
MFSD11	0.00E+00	0.00E+00
NUP93	0.00E+00	0.00E+00
ATP10D	0.00E+00	0.00E+00
C12orf4	0.00E+00	0.00E+00
EFTUD1	0.00E+00	0.00E+00

Figure 3

GTF3C3	0.00E+00	0.00E+00
H2AFY	0.00E+00	0.00E+00
KLC1	0.00E+00	0.00E+00
MGC29891	0.00E+00	0.00E+00
SNAPC3	0.00E+00	0.00E+00
VWF	0.00E+00	0.00E+00
ZZEF1	0.00E+00	0.00E+00
ACSS1	0.00E+00	0.00E+00
BRUNOL6	0.00E+00	0.00E+00
EYA2	0.00E+00	0.00E+00
ITPR3	0.00E+00	0.00E+00
MLL3	0.00E+00	0.00E+00
ORC2L	0.00E+00	0.00E+00
PCTK1	0.00E+00	0.00E+00
RBM33	0.00E+00	0.00E+00
TNS1	0.00E+00	0.00E+00
FAM120A	0.00E+00	0.00E+00
FLJ10986	0.00E+00	0.00E+00
CTSC	6.68E-302	9.13E-300
SETD4	8.65E-300	1.16E-297
UAP1	1.16E-293	1.52E-291
ATP2C2	2.78E-292	3.60E-290
PSMF1	4.83E-292	6.20E-290
CNTN5	7.41E-292	9.44E-290
LONRF2	3.58E-290	4.52E-288
DGKH	5.82E-285	7.16E-283
NFYC	2.68E-284	3.28E-282
FLJ20294	3.29E-284	3.98E-282
ZFYVE21	1.52E-283	1.82E-281
HECTD2	6.34E-282	7.56E-280
WASF3	4.99E-276	5.81E-274
KNTC1	8.88E-273	1.03E-270
MPPED2	1.10E-265	1.24E-263

Figure 3 Continued

LRRC48	6.58E-260	7.32E-258
EP400	7.62E-255	8.23E-253
KCTD10	1.02E-244	1.04E-242
SUSD1	2.04E-238	2.05E-236
TNFAIP8	3.89E-237	3.89E-235
FLJ10324	1.84E-235	1.80E-233
DIO1	1.11E-232	1.08E-230
ARHGAP6	1.22E-231	1.18E-229
MYO1D	8.30E-229	7.93E-227
PER2	1.55E-228	1.47E-226
ANXA9	3.78E-228	3.56E-226
MYH14	1.26E-225	1.17E-223
LTBP2	8.02E-224	7.33E-222
AOX1	3.41E-219	3.04E-217
PAK3	9.65E-219	8.56E-217
CDK7	6.41E-218	5.62E-216
SLC39A9	6.37E-217	5.55E-215
SRF	3.30E-208	2.79E-206
LRRC50	2.08E-205	1.75E-203
FTH1	2.32E-204	1.93E-202
DOPEY2	1.22E-203	1.01E-201
EGR2	7.02E-202	5.78E-200
ITGA2	8.74E-202	7.15E-200
FLJ21511	8.30E-200	6.72E-198
KHDRBS2	1.06E-194	8.28E-193
ABCC3	2.40E-191	1.85E-189
PCSK6	4.70E-190	3.55E-188
PDE6B	5.87E-190	4.42E-188
AUTS2	2.16E-183	1.58E-181
KIAA1324	2.64E-182	1.92E-180
ETV5	5.10E-182	3.69E-180
POLE2	2.98E-179	2.13E-177
CPEB2	3.75E-178	2.67E-176

Figure 3 Continued

PKHD1L1	3.58E-176	2.52E-174
CHRND	5.54E-176	3.88E-174
ZW10	3.17E-175	2.21E-173

Figure 3 Continued

Gene	DE p-value	FDR DE p-value	Fold-change Malignant/Benign
SEMA3D	1.02E-08	3.23E-04	-11.18
PDLIM4	4.57E-08	3.82E-04	3.51
LRP1B	7.45E-08	4.15E-04	-14.82
PLCD3	7.52E-08	4.15E-04	4.97
FN1	9.57E-08	4.15E-04	10.71
KIT	1.35E-07	4.43E-04	-4.75
SPOCK1	1.45E-07	4.43E-04	5.04
EPS8	1.57E-07	4.44E-04	3.17
STK32A	1.87E-07	4.61E-04	5.09
IHPK3	1.94E-07	4.72E-04	-3.06
TCID-2526806	2.08E-07	4.80E-04	2.86
MYEF2	2.11E-07	4.80E-04	3.61
ARHGAP24	2.32E-07	4.89E-04	-2.84
MPPED2	3.43E-07	5.56E-04	-4.49
TGFA	3.59E-07	5.56E-04	4.13
KHDRBS2	4.99E-07	6.53E-04	-4.28
TPO	7.17E-07	7.72E-04	-5.28
LGALS3	7.18E-07	7.72E-04	3.77
SLC26A4	9.16E-07	8.86E-04	-4.26
GALE	9.62E-07	9.19E-04	3.46
GABRB2	1.18E-06	1.03E-03	10.65
KLHDC8A	1.35E-06	1.10E-03	4.64
CDH3	1.72E-06	1.22E-03	6.67
GALNT7	1.75E-06	1.22E-03	3.78
CYSLTR2	2.53E-06	1.56E-03	7.40
RAG1	3.49E-06	1.89E-03	-9.03
PSD3	4.08E-06	2.04E-03	4.19
FABP4	4.18E-06	2.04E-03	-11.06
MATN2	4.23E-06	2.05E-03	-2.87

Figure 4

TRPC5	4.54E-06	2.14E-03	3.77
LRP2	4.78E-06	2.17E-03	-4.40
MT1F	4.93E-06	2.20E-03	-5.00
CDH16	5.19E-06	2.28E-03	-2.86
METTL7B	6.09E-06	2.52E-03	3.20
SYTL5	7.23E-06	2.82E-03	3.10
CAMK2N1	7.45E-06	2.84E-03	3.82
LIPH	7.70E-06	2.90E-03	36.34
AGTR1	8.16E-06	2.99E-03	-3.41
P2RY13	8.47E-06	3.06E-03	3.39
SLC26A7	9.12E-06	3.22E-03	-3.43
LRRC7	9.97E-06	3.38E-03	-2.91
SPINK5	1.06E-05	3.53E-03	-4.56
TMEM166	1.34E-05	4.04E-03	6.87
SCG5	1.46E-05	4.27E-03	5.53
NPC2	1.52E-05	4.37E-03	2.78
CD36	1.55E-05	4.41E-03	-4.41
RAG2	1.61E-05	4.49E-03	-13.38
COL9A3	1.64E-05	4.55E-03	-6.08
ELMO1	1.97E-05	5.17E-03	-2.92
PLA2R1	2.03E-05	5.26E-03	-4.85
7A5	2.04E-05	5.28E-03	3.11
MRO	2.17E-05	5.45E-03	-3.35
DGKI	2.45E-05	5.93E-03	-3.38
TUSC3	2.58E-05	6.13E-03	4.30
TFF3	2.65E-05	6.21E-03	-5.45
TNFRSF10C	2.78E-05	6.38E-03	2.85
PROS1	2.80E-05	6.40E-03	2.72
TCID-3430620	2.91E-05	6.55E-03	-3.96
ITGA2	3.09E-05	6.80E-03	3.42
GPM6A	3.10E-05	6.80E-03	-3.86
CDON	3.28E-05	7.05E-03	-2.73

Figure 4 Continued

ARNTL	3.49E-05	7.36E-03	2.84
GDF15	3.58E-05	7.49E-03	6.64
NRCAM	3.77E-05	7.75E-03	4.02
GSTM3	3.87E-05	7.90E-03	-2.71
ADAMTS9	3.89E-05	7.91E-03	2.85
MED12L	4.20E-05	8.33E-03	2.81
LONRF2	4.29E-05	8.45E-03	3.73
DNASE1L3	4.35E-05	8.54E-03	-3.08
TIPARP	4.53E-05	8.72E-03	2.76
DPP6	4.56E-05	8.73E-03	-3.90
DPP4	4.70E-05	8.89E-03	12.09
TMEM100	4.71E-05	8.90E-03	4.37
RYR2	4.75E-05	8.93E-03	-3.76
CLDN1	4.76E-05	8.93E-03	7.83
RXRG	4.80E-05	8.97E-03	3.09
QPCT	4.82E-05	9.00E-03	3.46
SAMD4A	5.00E-05	9.21E-03	2.80
PKHD1L1	5.21E-05	9.49E-03	-7.12
MET	5.26E-05	9.55E-03	3.10
FAM114A1	5.30E-05	9.60E-03	2.79
SCEL	5.53E-05	9.85E-03	11.17
SLA	1.22E-04	1.58E-02	-2.99
RIMS2	2.01E-04	2.13E-02	2.97
KIAA0408	2.44E-04	2.38E-02	2.75
IL1RAP	2.50E-04	2.42E-02	2.74
SCNN1A	2.72E-04	2.51E-02	2.98
LIFR	3.13E-04	2.74E-02	-2.96
FAM20A	4.06E-04	3.18E-02	2.98
PHF16	6.01E-04	4.00E-02	2.75
SLC5A8	6.35E-04	4.14E-02	-2.98
ODZ1	6.43E-04	4.16E-02	2.97
DLG2	7.11E-04	4.40E-02	-2.74
TBX22	7.82E-04	4.63E-02	-2.73

Figure 4 Continued

LAMB3	9.79E-04	5.30E-02	3.00
AQP4	1.16E-03	5.85E-02	-2.76
SLPI	1.22E-03	6.05E-02	2.93
COL13A1	1.34E-03	6.37E-02	2.97
SULF1	2.33E-03	8.77E-02	2.96
CYP1B1	2.65E-03	9.43E-02	2.99

Figure 4 Continued

Gene	DE FDR p-value	Alt. Exon FDR p-value	Fold-Change Malignant/Benign	Fold-Change Malignant/Normal	Fold-Change Benign/Normal
PLA2R1	9.27E-08	1.03E-54	-1.93	-3.36	-1.74
MYEF2	1.14E-07	9.58E-27	1.69	2.42	1.43
LRP1B	2.60E-06	0.00E+00	-1.93	-2.42	-1.25
MPPED2	3.47E-06	1.24E-263	-2.05	-2.32	-1.13
KHDRBS2	9.85E-06	8.28E-193	-2.03	-2.63	-1.30
FN1	1.02E-05	7.02E-127	3.96	5.84	1.47
SPATS2	1.10E-05	2.79E-04	1.13	1.56	1.38
KIT	1.12E-05	0.00E+00	-1.88	-2.10	-1.12
MATN2	1.26E-05	1.21E-21	-1.91	-3.12	-1.63
C9orf58	1.31E-05	3.87E-16	-1.29	-1.90	-1.47
ChGn	1.41E-05	5.54E-23	-2.27	-2.99	-1.32
ANGPTL1	1.88E-05	4.11E-32	-1.44	-2.00	-1.39
FABP4	2.42E-05	6.34E-105	-3.31	-5.39	-1.63
XPR1	4.31E-05	9.06E-05	1.53	2.09	1.36
TPO	5.83E-05	0.00E+00	-3.18	-4.29	-1.35
C10orf79	5.96E-05	5.75E-43	-1.19	-1.68	-1.42
TSC22D1	6.31E-05	6.19E-11	1.89	1.37	-1.38
GALNT7	8.40E-05	5.15E-10	1.82	2.08	1.14
SLC26A4	8.70E-05	2.69E-05	-3.22	-4.27	-1.33
CYSLTR2	1.08E-04	3.75E-27	1.75	1.67	-1.05
GABRB2	1.15E-04	1.80E-56	2.45	2.60	1.06
NRCAM	1.15E-04	3.42E-17	1.80	3.16	1.76
ADH1C	1.16E-04	3.48E-18	-1.12	-1.60	-1.43
DPP6	1.23E-04	0.00E+00	-1.53	-2.45	-1.60
LINGO2	1.50E-04	3.74E-170	-1.32	-1.77	-1.34
SDC4	1.55E-04	8.65E-48	2.13	1.95	-1.09
ZFPM2	1.55E-04	5.60E-04	-1.17	-1.71	-1.46
ARHGAP24	2.27E-04	5.27E-18	-1.76	-2.04	-1.16
ARMCX3	2.28E-04	5.35E-03	1.50	1.68	1.12

Figure 5

RUNX1T1	2.38E-04	1.58E-116	-1.18	-1.56	-1.32
C11orf74	2.49E-04	6.94E-07	-1.73	-2.50	-1.45
LRP2	3.29E-04	2.10E-93	-2.14	-2.07	1.03
NPC2	3.64E-04	5.21E-19	1.39	1.61	1.16
PLSCR4	3.69E-04	6.94E-12	-1.31	-1.77	-1.35
STK32A	4.12E-04	3.12E-12	2.11		
TNIK	5.27E-04	2.62E-35	1.34	1.99	1.48
ANKRD37	5.34E-04	2.62E-93	-1.27	-1.61	-1.27
SCG5	7.03E-04	1.47E-03	3.16	2.81	-1.13
TBC1D4	7.08E-04	1.51E-16	-1.61		
DPP4	7.70E-04	3.02E-138	2.55	3.30	1.29
ELMO1	8.04E-04	7.58E-08	-1.75	-1.75	1.00
PGCP	8.07E-04	9.61E-03	-1.47	-1.99	-1.35
SDC2	9.39E-04	1.03E-10	-1.67	-2.64	-1.58
FAM20A	9.45E-04	1.44E-127	1.29	1.61	1.25
METTL7B	9.70E-04	2.26E-13	1.58	1.65	1.05
MAP2	9.94E-04	5.51E-08	1.50	1.58	1.05
CD36	1.04E-03	0.00E+00	-2.03	-1.95	1.04
CRABP1	1.09E-03	1.16E-10	-2.65	-6.83	-2.58
EFEMP1	1.10E-03	4.91E-04	-1.56	-2.43	-1.56
DCBLD2	1.11E-03	1.08E-06	1.59	1.68	1.05
FLRT2	1.14E-03	1.66E-128	-1.13	-1.61	-1.43
ITGA2	1.23E-03	7.15E-200	1.73	2.20	1.27
EGR1	1.51E-03	5.74E-13	-1.30	-2.55	-1.97
ASCC3	1.66E-03	4.30E-04	1.21	1.64	1.35
EGR2	1.66E-03	5.78E-200	-1.75	-3.38	-1.93
MET	1.72E-03	4.65E-09	2.09	2.32	1.11
CLDN16	1.74E-03	1.27E-19	2.48	3.55	1.44
HMGA2	1.82E-03	1.78E-11	1.47	1.79	1.21
CENPJ	2.13E-03	0.00E+00	-1.44	-1.60	-1.12
GPR125	2.17E-03	1.04E-11	-1.43	-1.67	-1.17
RABL3	2.21E-03	2.31E-21	-1.97	-1.94	1.02
CD63	2.42E-03	7.85E-04	1.40	1.60	1.14

Figure 5 Continued

P4HA2	2.49E-03	3.08E-13	1.71		
ETV5	2.56E-03	3.69E-180	1.56	1.96	1.26
ITM2A	2.57E-03	3.01E-07	-1.56	-1.99	-1.28
C9orf52	2.57E-03	3.76E-08	1.30	1.83	1.40
7A5	2.62E-03	5.07E-17	1.61		
ANKS1B	2.71E-03	0.00E+00	-1.31	-1.68	-1.29
THRAP1	2.72E-03	1.06E-05	1.34	1.59	1.18
PROS1	2.79E-03	2.25E-15	1.64	1.95	1.19
NFE2L3	2.83E-03	2.91E-06	1.44	2.01	1.39
CYR61	2.83E-03	2.07E-07	-1.92	-2.58	-1.35
ERO1LB	2.99E-03	2.24E-03	-1.61		
ACO1	3.03E-03	3.40E-10	1.32	1.73	1.31
PKHD1L1	3.31E-03	2.52E-174	-2.55	-3.84	-1.50
DLG2	3.32E-03	2.35E-85	-1.44	-2.02	-1.40
C9orf61	3.39E-03	5.60E-08	-1.81	-2.04	-1.12
DEPDC6	4.09E-03	9.94E-11	-1.53	-1.69	-1.10
LRRC7	4.12E-03	7.23E-155	-1.48	-1.73	-1.17
MLLT3	4.64E-03	4.64E-03	-1.41	-1.71	-1.21
TUSC3	4.69E-03	1.31E-11	1.91		
ALDH1A1	4.74E-03	4.61E-08	-1.81	-2.15	-1.19
FBLN5	4.82E-03	3.18E-09	-1.26	-1.72	-1.37
SLA	4.90E-03	4.03E-03	-1.93	-1.60	1.21
LONRF2	4.97E-03	4.52E-288	1.85	1.49	-1.24
PSD3	5.13E-03	6.97E-19	1.43	1.91	1.33
LIFR	5.23E-03	2.95E-17	-1.77	-2.34	-1.32
C7orf24	5.88E-03	4.91E-05	1.58	1.96	1.24
S100A2	6.41E-03	3.25E-115	2.42	1.39	-1.74
WDR72	6.43E-03	1.50E-16	-1.92	-2.51	-1.31
MT1G	6.55E-03	1.96E-05	-2.49	-3.07	-1.23
LONRF2	6.60E-03	9.73E-05	1.91		
SLC4A4	6.75E-03	0.00E+00	-1.72	-1.76	-1.03
MT1H	6.86E-03	8.57E-09	-1.58	-1.83	-1.16
DNAJB4	6.86E-03	1.92E-04	-1.31	-2.13	-1.62

Figure 5 Continued

CTGF	6.86E-03	1.42E-11	-1.92	-2.83	-1.48
SERPINA1	6.87E-03	3.07E-04	2.89	3.08	1.07
RHOBTB3	6.90E-03	0.00E+00	1.68	1.99	1.18
QPCT	6.90E-03	5.26E-07	2.01	2.09	1.04
TMEM171	9.30E-03	7.78E-04	-1.51	-2.92	-1.93

Figure 5 Continued

TCID	GENE_na29
2337524	2337524
2357193	2357193
2383807	2383807
2406391	2406391
2472880	2472880
2489140	2489140
2494151	2494151
2506693	2506693
2641232	2641232
2649710	2649710
2652217	2652217
2832019	2832019
2908499	2908499
2908502	2908502
3092561	3092561
3107603	3107603
3139557	3139557
3153400	3153400
3184925	3184925
3253452	3253452
3321980	3321980
3398455	3398455
3511158	3511158
3619197	3619197
3749600	3749600
3777770	3777770
3881010	3881010
3893716	3893716
3895675	3895675
3958399	3958399
3289445	A1CF
3443348	A2M
2558150	AAK1
3697015	AARS
3070183	AASS
3719362	AATF
3218528	ABCA1
2756309	ABCA10
3768880	ABCA10
2756309	ABCA11P
3768880	ABCA11P
3768969	ABCA5
3768791	ABCA6
3815416	ABCA7
3768627	ABCA8
3768627	ABCA9
3768703	ABCA9
3060117	ABCB1
3060182	ABCB1
2459924	ABCB10
3060117	ABCB4
2599993	ABCB6
4012949	ABCB7
3690470	ABCC11

TCID	GENE_na29
3914786	ABCC13
3260447	ABCC2
3726691	ABCC3
3446919	ABCC9
3450861	ABCD2
2777276	ABCG2
2550755	ABCG5
2474265	ABHD1
3535307	ABHD12B
3607447	ABHD2
2523689	ABI2
2686458	ABI3BP
3307939	ABLIM1
3739962	ABR
3368940	ABTB2
3754469	ACACA
3430959	ACACB
3432030	ACAD10
2695648	ACAD11
2641341	ACAD9
2597347	ACADL
3708306	ACADVL
2712040	ACAP2
3723317	ACBD4
3279058	ACBD7
3328069	ACCSL
3730601	ACE
4000605	ACE2
3164312	ACER2
3528994	ACIN1
3528895	ACIN1
3757433	ACLY
3013952	ACN9
3166477	ACO1
2394626	ACOT7
4002741	ACOT9
3771215	ACOX1
2759857	ACOX3
2645387	ACPL2
3981164	ACRC
3603199	ACSBG1
3726406	ACSF2
2796553	ACSL1
4017810	ACSL4
3651294	ACSM5
3901696	ACSS1
3424218	ACSS3
2459837	ACTA1
3299504	ACTA2
3569814	ACTN1
2386943	ACTN2
3861503	ACTN4
3832643	ACTN4
3304406	ACTR1A

TCID	GENE_na29
2501697	ACTR3
2676901	ACTR8
2582562	ACVR1
3415148	ACVR1B
2509557	ACVR2A
3415109	ACVRL1
2623441	ACY1
3572263	ACYP1
3702382	ADAD2
3311832	ADAM12
2539821	ADAM17
3011492	ADAM22
3927446	ADAMTS1
3641633	ADAMTS17
3700158	ADAMTS18
2889916	ADAMTS2
3927480	ADAMTS5
2859601	ADAMTS6
2680046	ADAMTS9
2977471	ADAT2
2800711	ADCY2
3558168	ADCY4
3453252	ADCY6
3153716	ADCY8
3775906	ADCYAP1
2558736	ADD2
3263555	ADD3
2779271	ADH1A
2779231	ADH1A
2779199	ADH1A
2779271	ADH1B
2779231	ADH1B
2779199	ADH1B
2779271	ADH1C
2779231	ADH1C
2779124	ADH4
2387711	ADH5
2779095	ADH5
2779163	ADH6
3252170	ADK
3320123	ADM
3248824	ADO
2375596	ADORA1
3940001	ADORA2A
3711869	ADORA2B
2427981	ADORA3
3265047	ADRB1
4049835	ADRB3
3940631	ADRBK2
2464353	ADSS
3607232	AEN
2834957	AFAP1L1
3307851	AFAP1L2
2399743	AFARP1

Figure 6

TCID	GENE_na29
2734784	AFF1
3554592	AFF1
2875555	AFF4
2533670	AGAP1
3031880	AGAP3
3606682	AGBL1
3372420	AGBL2
2949830	AGER
2530599	AGFG1
3083936	AGPAT5
3095815	AGPAT6
2734047	AGPAT9
3039791	AGR2
3039830	AGR3
3695726	AGRP
3212728	AGTPBP1
2647015	AGTR1
2889486	AGXT2L2
3023384	AHCYL2
2975385	AHI1
3375735	AHNAK
3581221	AHNAK2
2991233	AHR
3545466	AHSA1
2555277	AHSA2
3522398	AIDA
2381876	AIDA
2457573	AIDA
4042837	AIDA
3191877	AIF1L
2439554	AIM2
3226138	AK1
2340315	AK3L1
3728097	AKAP1
3749086	AKAP10
3487220	AKAP11
2931569	AKAP12
3606304	AKAP13
3184408	AKAP2
4008170	AKAP4
3540068	AKAP5
2925724	AKAP7
3853299	AKAP8
3012381	AKAP9
2969201	AKD2
3073981	AKR1B1
3274758	AKR1C1
3274758	AKR1C2
3233049	AKR1C3
3232944	AKR1CL2
2399743	AKR7A3
2399743	AKR7L
4009849	ALAS2
3838522	ALDH16A1

TCID	GENE_na29
3209726	ALDH1A1
3611625	ALDH1A3
3169331	ALDH1B1
3714068	ALDH3A2
3337329	ALDH3B1
3379091	ALDH3B1
3337329	ALDH3B2
3379091	ALDH3B2
3571727	ALDH6A1
2873785	ALDH7A1
2975257	ALDH8A1
3750767	ALDOC
3990566	ALG11
3490504	ALG11
3965393	ALG12
2424148	ALG14
2708407	ALG3
2339682	ALG6
3383164	ALG8
3391149	ALG9
2546409	ALK
3389878	ALKBH8
2488785	ALMS1
2488785	ALMS1P
3709417	ALOX15B
3244622	ALOX5
2532314	ALPI
2532294	ALPI
3605884	ALPK3
2532314	ALPP
2532294	ALPP
2532272	ALPP
2532294	ALPPL2
2532272	ALPPL2
2594773	ALS2CR12
2852742	AMACR
3371544	AMBRA1
3692856	AMFR
3393670	AMICA1
3452478	AMIGO2
4017961	AMMECR1
3410322	AMN1
4018454	AMOT
2696309	AMOTL2
3046739	AMPH
2571075	ANAPC1
2788143	ANAPC10
3527597	ANG
3572782	ANGEL1
3148463	ANGPT1
3122489	ANGPT2
2445982	ANGPTL1
3819474	ANGPTL4
3388517	ANGPTL5

TCID	GENE_na29
3850020	ANGPTL6
2740067	ANK2
3290875	ANK3
3598199	ANKDD1A
3727787	ANKFN1
3741997	ANKFY1
2849469	ANKH
3349535	ANKK1
3525679	ANKRD10
3778252	ANKRD12
3431376	ANKRD13A
3716151	ANKRD13B
2773023	ANKRD17
3205834	ANKRD18A
3205834	ANKRD18B
2565559	ANKRD23
3282117	ANKRD26
2356273	ANKRD35
2564816	ANKRD36
2565935	ANKRD36
2564816	ANKRD36B
2565935	ANKRD36B
2754673	ANKRD37
3146661	ANKRD46
3876142	ANKRD5
2857488	ANKRD55
2916825	ANKRD6
2904329	ANKS1A
3467351	ANKS1B
3678279	ANKS3
3217361	ANKS6
3441542	ANO2
3428333	ANO4
3323748	ANO5
2487082	ANTXR1
2774971	ANTXR2
3286975	ANUBL1
3174816	ANXA1
3627248	ANXA2
3167110	ANXA2
3627248	ANXA2P1
2790109	ANXA2P1
3167110	ANXA2P2
3249171	ANXA2P3
2732844	ANXA3
2487412	ANXA4
2784027	ANXA5
2881747	ANXA6
2358591	ANXA9
3046062	AOAH
3722195	AOC3
2522247	AOX1
3754677	AP1GBP1
3016177	AP1S1

Figure 6 continued

TCID	GENE_na29
2601287	AP1S3
3718682	AP2B1
2655476	AP2M1
2863730	AP3B1
3636216	AP3B2
3295032	AP3M1
3096007	AP3M2
2455418	AP3S1
3638665	AP3S2
2428855	AP4B1
3593770	AP4E1
2766893	APBB2
2878368	APBB3
2824198	APC
2622196	APEH
2434341	APH1A
3597521	APH1B
3369249	APIP
2486851	APLF
3356116	APLP2
2361584	APOA1BP
3945572	APOBEC3C
3945651	APOBEC3F
3945651	APOBEC3G
3835891	APOC1
4054204	APOD
3944404	APOL1
3959350	APOL3
2902531	APOM
4002809	APOO
3983105	APOOL
2833924	APOOL
2625606	APPL1
3469319	APPL2
3203311	APTX
3802396	AQP4
3595594	AQP9
3617757	AQR
3381241	ARAP1
2765590	ARAP2
2731542	AREG
3453370	ARF3
3962587	ARFGAP3
3139035	ARFGEF1
3888055	ARFGEF2
2747893	ARFIP1
2925841	ARG1
3524618	ARGLU1
2746693	ARHGAP10
3283920	ARHGAP12
2508611	ARHGAP15
2973694	ARHGAP18
3302187	ARHGAP19
3390641	ARHGAP20

TCID	GENE_na29
2734421	ARHGAP24
2833286	ARHGAP26
3777263	ARHGAP28
2423829	ARHGAP29
3531479	ARHGAP5
3999568	ARHGAP6
3948259	ARHGAP8
3445786	ARHGDIB
3642747	ARHGDIG
3352503	ARHGEF12
2437801	ARHGEF2
2677723	ARHGEF3
2505833	ARHGEF4
3029646	ARHGEF5
3029646	ARHGEF5L
3501661	ARHGEF7
3537884	ARID4A
2461786	ARID4B
3600744	ARIH1
2621827	ARIH2
2842530	ARL10
2632453	ARL13B
3767169	ARL17P1
3334783	ARL2
3304475	ARL3
2931391	ARL4A
2990464	ARL4A
2724853	ARL4A
3683037	ARL6IP1
2628682	ARL6IP5
2451139	ARL8A
2608765	ARL8B
3017080	ARMC10
3238702	ARMC3
2644461	ARMC8
2531779	ARMC9
3984945	ARMCX3
4015838	ARMCX6
3321150	ARNTL
3409127	ARNTL2
3471198	ARPC3
3188993	ARPC5L
2616596	ARPP-21
2866704	ARRDC3
3768474	ARSG
2782694	ARSJ
2731928	ART3
3445723	ART4
3359881	ART5
3261923	AS3MT
3395464	ASAM
3153428	ASAP1
2468811	ASAP2
2553262	ASB3

TCID	GENE_na29
3191074	ASB6
2966636	ASCC3
3429008	ASCL1
3743371	ASGR1
2437417	ASH1L
3094447	ASH2L
3966597	ASMT
3137530	ASPH
3214845	ASPN
2695295	ASTE1
3881874	ASXL1
2544925	ASXL2
3069399	ASZ1
3299255	ATAD1
3151534	ATAD2
3716893	ATAD5
3310413	ATE1
2588066	ATF2
2379132	ATF3
2949622	ATF6B
3647827	ATF7IP2
2818212	ATG10
3769779	ATG12
3578278	ATG2B
2339511	ATG4C
2526759	ATIC
2548776	ATL2
3347658	ATM
3390143	ATM
3670668	ATMIN
2726072	ATP10D
2654855	ATP11B
2711225	ATP13A4
2711205	ATP13A4
2353477	ATP1A1
2645764	ATP1B3
3431483	ATP2A2
3464983	ATP2B1
2375706	ATP2B4
2642325	ATP2C1
2695295	ATP2C1
3671727	ATP2C2
2351817	ATP5F1
2714200	ATP5I
3916576	ATP5J
3535125	ATP5S
3996381	ATP6AP1
3105749	ATP6V0D2
2841284	ATP6V0E1
2636589	ATP6V1A
3088544	ATP6V1B2
2469529	ATP6V1C2
2949038	ATP6V1G2
3982423	ATP7A

Figure 6 continued

TCID	GENE_na29
2767378	ATP8A1
3482274	ATP8A2
3809826	ATP8B1
3712835	ATPAF2
3617920	ATPBD4
2698844	ATR
3874313	ATRN
4013224	ATRX
3948754	ATXN10
3471588	ATXN2
3576889	ATXN3
2627390	ATXN7
2456849	AURKA
2456849	AURKAPS1
3006572	AUTS2
2996033	AVL9
3459722	AVPR1A
3063589	AZGP1
2667181	AZI2
3147591	AZIN1
2386418	B3GALNT2
2449104	B3GALT2
3375935	B3GAT3
3824596	B3GNT3
3475511	B3GNT4
3418394	B4GALNT1
3400236	B4GALNT3
2440664	B4GALT3
3908963	B4GALT5
3803120	B4GALT6
3110217	BAALC
3393257	BACE1
3921933	BACE2
3981120	BAG1
2911372	BAG2
3267314	BAG3
3094494	BAG4
3924929	BAGE
3924929	BAGE2
3924929	BAGE3
3924929	BAGE4
3924929	BAGE5
3589947	BAHD1
2912416	BAI3
3737697	BAIAP2
3240452	BAMBI
2737596	BANK1
2949038	BAT1
2367154	BAT2D1
2949256	BAT5
3838067	BAX
3560711	BAZ1A
3056044	BAZ1B
3457947	BAZ2A

TCID	GENE_na29
2583014	BAZ2B
3324453	BBOX1
3600960	BBS4
2996321	BBS9
2634965	BBX
3835777	BCAM
3018535	BCAP29
4026669	BCAP31
3729569	BCAS3
3311775	BCCIP
3269662	BCCIP
3454147	BCDIN3D
2420808	BCL10
2554975	BCL11A
3811339	BCL2
3635198	BCL2A1
3902489	BCL2L1
2500275	BCL2L11
3936256	BCL2L13
3405207	BCL2L14
3386737	BCL7B
2356818	BCL9
3348940	BCO2
2814527	BDP1
3758157	BECN1
2411799	BEND5
4016308	BEX1
4016308	BEX2
3649245	BFAR
3899111	BFSP1
2608725	BHLHE40
3448088	BHLHE41
2817251	BHMT
2817251	BHMT2
3951927	BID
3346548	BIRC3
3772187	BIRC5
2476219	BIRC6
3893250	BIRC7
3499585	BIVM
3608298	BLM
3751830	BLMH
3301713	BLNK
3303392	BLOC1S2
2366490	BLZF1
3619229	BMF
3238491	BMI1
3089215	BMP1
2774817	BMP2K
2958172	BMP5
2893895	BMP6
2331558	BMP8A
2331511	BMP8A
2331511	BMP8B

TCID	GENE_na29
3256074	BMPR1A
2523213	BMPR2
3936817	BMS1
2841528	BNIP1
3314040	BNIP3
2761285	BOD1L
2536625	BOK
3683050	BOLA2
2593838	BOLL
3732448	BPTF
2877257	BRD8
2798915	BRD9
2442858	BRP44
3842059	BRSK1
3267678	BRWD2
4013730	BRWD3
3333595	BSCL2
3854417	BST2
3636470	BTBD1
3363645	BTBD10
3430462	BTBD11
3554592	BTBD6
3577277	BTBD7
2952497	BTBD9
2773545	BTC
2553771	BTF3
2375664	BTG2
3926080	BTG3
2899372	BTN3A1
2899298	BTN3A1
2899372	BTN3A2
2899298	BTN3A2
2899372	BTN3A3
2899298	BTN3A3
2844859	BTNL8
3261165	BTRC
3014742	BUD31
3764289	BZRAP1
2690012	BZW1
2522439	BZW1
2690012	BZW1L1
2522439	BZW1L1
3286776	C10orf10
3279089	C10orf111
3307795	C10orf118
3309755	C10orf119
3259087	C10orf129
3259263	C10orf131
3231846	C10orf139
3280787	C10orf140
3275132	C10orf18
3244539	C10orf25
3261886	C10orf26
3260099	C10orf28

Figure 6 continued

TCID	GENE_na29
3261923	C10orf32
3309124	C10orf46
3294959	C10orf55
3254337	C10orf57
3254488	C10orf58
3241601	C10orf68
3288518	C10orf72
3305198	C10orf79
3314720	C10orf92
3314720	C10orf93
3279410	C10orf97
3334847	C11orf2
3334446	C11orf20
3358112	C11orf35
3356417	C11orf44
3325052	C11orf46
3375999	C11orf48
3329537	C11orf49
3380996	C11orf51
3396144	C11orf61
3353441	C11orf63
3390143	C11orf65
2708855	C11orf72
3343252	C11orf73
3327166	C11orf74
3386737	C11orf75
3336486	C11orf80
3368707	C11orf91
3465188	C12orf12
3430389	C12orf23
3424379	C12orf26
3421824	C12orf28
3464622	C12orf29
3471819	C12orf30
3443434	C12orf33
3410384	C12orf35
3407849	C12orf39
3441215	C12orf4
3411234	C12orf40
3453177	C12orf41
3473331	C12orf49
3401756	C12orf5
3442249	C12orf53
3403077	C12orf57
3427282	C12orf63
3410322	C12orf72
3429857	C12orf75
3471073	C12orf76
3486956	C13orf15
3480681	C13orf3
3484117	C13orf33
3485740	C13orf36
3563372	C14orf104
3528994	C14orf119

TCID	GENE_na29
3550328	C14orf129
3550234	C14orf132
3563687	C14orf138
3573933	C14orf145
3573994	C14orf145
3566949	C14orf149
3543619	C14orf169
3569778	C14orf181
3571727	C14orf45
3543979	C14orf45
3540155	C14orf50
3554523	C14orf79
3554868	C14orf80
3569285	C14orf83
3633191	C15orf17
3623472	C15orf33
3629761	C15orf44
3641597	C15orf51
3619479	C15orf57
3643114	C16orf14
3649714	C16orf45
3701433	C16orf46
3695819	C16orf48
3655708	C16orf53
3644191	C16orf73
3693511	C16orf80
3678542	C16orf89
3774975	C17orf101
3744300	C17orf44
3712098	C17orf45
3710277	C17orf48
3708201	C17orf49
3724591	C17orf57
3744254	C17orf59
3766621	C17orf72
3769969	C17orf80
3735752	C17orf86
3742627	C17orf87
3740664	C17orf91
3803500	C18orf34
3791341	C18orf49
3793588	C18orf55
3795850	C18orf56
3798829	C18orf58
3828162	C19orf2
3817651	C19orf30
3832280	C19orf33
3868330	C19orf41
3822347	C19orf53
3862785	C19orf54
3864597	C19orf61
3839400	C19orf63
3850020	C19orf66
3837664	C19orf68

TCID	GENE_na29
2557549	C1D
4019967	C1GALT1C1
2406735	C1orf102
2443305	C1orf114
2381249	C1orf115
2453065	C1orf116
2369609	C1orf125
2407128	C1orf149
2431886	C1orf152
2391005	C1orf159
2320392	C1orf187
2436576	C1orf189
2371547	C1orf21
2406412	C1orf216
2369325	C1orf220
2364016	C1orf226
2371738	C1orf26
2436576	C1orf43
2369325	C1orf49
2358136	C1orf51
2381876	C1orf58
2402111	C1orf63
2389718	C1orf71
2359736	C1orf77
2336963	C1orf83
2438093	C1orf85
3236786	C1QL3
2852742	C1QTNF3
2719440	C1QTNF7
3403168	C1S
2902844	C2
3876084	C20orf103
3890109	C20orf108
3893072	C20orf11
3902764	C20orf112
3899495	C20orf12
3904797	C20orf132
3746881	C20orf191
3891723	C20orf197
3895679	C20orf27
3901665	C20orf3
3896174	C20orf30
3877221	C20orf7
3900091	C20orf74
3918104	C21orf63
3926138	C21orf91
3958045	C22orf30
3965102	C22orf34
3955357	C22orf36
3952703	C22orf39
3954764	C22orf43
3963676	C22orf9
3933331	C2CD2
3381702	C2CD3

Figure 6 continued

TCID	GENE_na29
2525682	C2orf21
2506335	C2orf27A
2506335	C2orf27B
2496628	C2orf29
2482230	C2orf30
2473831	C2orf39
2498274	C2orf40
2477372	C2orf56
2594313	C2orf60
2566383	C2orf64
2560317	C2orf65
2597273	C2orf67
2525852	C2orf67
2559494	C2orf7
2482440	C2orf73
2556017	C2orf86
2520069	C2orf88
3848039	C3
2662581	C3orf10
2627080	C3orf14
2688882	C3orf17
2612012	C3orf20
2663083	C3orf31
2641577	C3orf37
2619521	C3orf41
2610417	C3orf42
2700780	C3orf44
2627368	C3orf49
2636062	C3orf52
2674168	C3orf62
2677653	C3orf63
2681114	C3orf64
2902958	C4A
2902958	C4B
2758076	C4orf10
2734352	C4orf12
2770427	C4orf14
2791419	C4orf18
2765865	C4orf19
2717757	C4orf23
2743029	C4orf29
2739714	C4orf32
2766492	C4orf34
2753994	C4orf41
2730303	C4orf7
2715440	C4orf8
2875929	C5orf15
2805176	C5orf22
2829542	C5orf24
2855578	C5orf28
2831519	C5orf32
2853388	C5orf33
2855614	C5orf34
2882834	C5orf4

TCID	GENE_na29
2853642	C5orf42
2858793	C5orf43
3724591	C5orf45
2844479	C5orf45
2828564	C5orf56
2854915	C6
2951057	C6orf1
2941972	C6orf105
2951221	C6orf106
2927967	C6orf115
2986084	C6orf120
2901841	C6orf134
2956217	C6orf138
2909772	C6orf141
2960774	C6orf147
2960399	C6orf155
2916307	C6orf165
2966193	C6orf168
2973232	C6orf174
2984275	C6orf176
2969350	C6orf186
2974671	C6orf192
2939593	C6orf201
2902833	C6orf26
2985342	C6orf54
2945677	C6orf62
2930753	C6orf72
2931700	C6orf97
3060051	C7orf23
3041409	C7orf30
3005956	C7orf42
3048134	C7orf44
3022465	C7orf54
3060450	C7orf62
3011911	C7orf63
2995491	C7orf67
3037304	C7orf70
3194969	C8G
3085933	C8orf12
3124344	C8orf16
3107234	C8orf39
3095313	C8orf4
3096271	C8orf40
3130823	C8orf41
3121198	C8orf42
3101802	C8orf44
3101765	C8orf44
3086181	C8orf49
3151809	C8orf54
3119236	C8orf55
3089569	C8orf58
3118651	C8orf60
3099390	C8orf71
3086809	C8orf79

TCID	GENE_na29
3086774	C8orf79
3158812	C8orf82
3140478	C8orf84
3180717	C9orf102
3226709	C9orf114
2549092	C9orf126
3225224	C9orf126
3179872	C9orf129
3167684	C9orf131
3195083	C9orf142
3162529	C9orf150
3216931	C9orf156
3223903	C9orf31
3213847	C9orf33
3185618	C9orf43
3037304	C9orf51
3173974	C9orf61
3197231	C9orf68
3193018	C9orf7
3192580	C9orf9
3192912	C9orf96
3181240	C9orf97
3867264	CA11
3628498	CA12
3105506	CA13
3105600	CA2
3729419	CA4
3969855	CA5B
3969855	CA5BP
3137120	CA8
3168066	CA9
2531522	CAB39
3513752	CAB39L
3939707	CABIN1
3781531	CABLES1
3400730	CACNA1C
2624385	CACNA1D
3726618	CACNA1G
3643580	CACNA1H
3058991	CACNA2D1
2675315	CACNA2D2
3755580	CACNB1
3237396	CACNB2
2581349	CACNB4
3959787	CACNG2
3732092	CACNG4
3841184	CACNG6
2368198	CACYBP
3392332	CADM1
3864519	CADM4
2679406	CADPS
3364127	CALCA
3321592	CALCB
3456353	CALCOCO1

Figure 6 continued

TCID	GENE_na29
2591367	CALCRL
3025545	CALD1
3304767	CALHM2
2551924	CALM2
3599280	CALML4
3822049	CALR
3235516	CAMK1D
2782545	CAMK2D
3294854	CAMK2G
2400177	CAMK2N1
2823880	CAMK4
3229529	CAMSAP1
2374345	CAMSAP1L1
3420713	CAND1
3772776	CANT1
3861503	CAPN12
3590853	CAPN3
4018194	CAPN6
2612278	CAPN7
3831168	CAPNS1
3326183	CAPRIN1
2649182	CAPRIN1
3389450	CARD16
3389353	CARD17
3866958	CARD8
3820865	CARM1
2814693	CARTPT
3447798	CASC1
3266583	CASC2
3590014	CASC5
3013178	CASD1
3644541	CASKIN1
3389450	CASP1
3389353	CASP1
3389257	CASP12
2796484	CASP3
3389273	CASP4
2781693	CASP6
2916952	CASP8AP2
2429556	CASQ2
2638824	CASR
2868131	CAST
2821194	CAST
3326400	CAT
3378043	CATSPER1
2825514	CATSPER2
3020302	CAV1
3020273	CAV2
3293998	CBARA1
3704567	CBFA2T3
3665116	CBFB
3352070	CBL
3812864	CBLN2
3910724	CBLN4

TCID	GENE_na29
3919834	CBR3
3933923	CBS
2993639	CBX3
3456630	CBX5
3259367	CC2D2B
2619480	CCBP2
3686587	CCDC101
3251490	CCDC109A
2739160	CCDC109B
3941643	CCDC117
3987607	CCDC121
2545999	CCDC121
3858794	CCDC123
2860614	CCDC125
2992963	CCDC126
2670903	CCDC13
3822287	CCDC130
2692573	CCDC14
2560149	CCDC142
3765167	CCDC144A
3748400	CCDC144A
3009838	CCDC146
2582701	CCDC148
2855285	CCDC152
2423264	CCDC18
3367036	CCDC34
2622026	CCDC36
3731228	CCDC45
2641449	CCDC48
2657981	CCDC50
3468225	CCDC53
2343170	CCDC55
3434193	CCDC64
3413643	CCDC65
3344685	CCDC67
3808745	CCDC68
2881860	CCDC69
3241601	CCDC7
2425173	CCDC76
2348792	CCDC76
2688813	CCDC80
3387771	CCDC82
3351733	CCDC84
2553771	CCDC88A
2773407	CCDC90B
3817400	CCDC94
2759393	CCDC96
2840002	CCDC99
2948821	CCHCR1
3718204	CCL13
3753966	CCL14
3753966	CCL15
3753956	CCL16
3204285	CCL19

TCID	GENE_na29
3204301	CCL21
2855542	CCL28
3754070	CCL3
3754070	CCL3L1
3754070	CCL3L3
3485674	CCNA1
2741768	CCNA2
2966371	CCNC
3380065	CCND1
3338192	CCND1
3401704	CCND2
2953866	CCND3
2838598	CCNG1
3259400	CCNJ
2864578	CCNJL
2702307	CCNL1
4041923	CCNL2
2391532	CCNL2
3453218	CCNT1
2507209	CCNT2
2620736	CCR9
3213530	CCRK
3336351	CCS
3421630	CCT2
3003193	CCT6A
3003193	CCT6P1
3928070	CCT8
2913694	CD109
3316344	CD151
2432714	CD160
3442706	CD163
3835035	CD177
2860178	CD180
3655109	CD19
2362180	CD1A
2353669	CD2
2636125	CD200
3830359	CD22
4035833	CD24
3161082	CD274
3601229	CD276
2909404	CD2AP
3770305	CD300A
3770305	CD300C
3770361	CD300LF
2583254	CD302
2453307	CD34
3010503	CD36
3838385	CD37
3393744	CD3D
3836243	CD3EAP
3865378	CD3EAP
3992575	CD40LG
3326635	CD44

Figure 6 continued

TCID	GENE_na29
2377427	CD46
2687739	CD47
2440354	CD48
3332729	CD5
2326463	CD52
2351572	CD53
2377229	CD55
3368707	CD59
3457160	CD63
3443868	CD69
2881370	CD74
3834502	CD79A
3402315	CD9
2635741	CD96
3822657	CD97
3966836	CD99
3489350	CDADC1
3235461	CDC123
2348896	CDC14A
3503164	CDC16
2857042	CDC20B
3221543	CDC26
3760625	CDC27
2969467	CDC2L6
2921086	CDC40
2324634	CDC42
3119339	CDC42
2459042	CDC42BPA
3580498	CDC42BPB
3335070	CDC42EP2
3770029	CDC42EP4
2434776	CDC42SE1
3720896	CDC6
2346399	CDC7
2372967	CDC73
3402874	CDCA3
2992243	CDCA7L
3040897	CDCA7L
2671728	CDCP1
3694657	CDH11
3671202	CDH13
3695315	CDH16
3811949	CDH19
3802602	CDH2
3251068	CDH23
3666366	CDH3
2805078	CDH6
3417146	CDK2
3476097	CDK2AP1
3458783	CDK4
3223425	CDK5RAP2
2813481	CDK7
3482498	CDK8
3563861	CDKL1

TCID	GENE_na29
2773719	CDKL2
2905169	CDKN1A
3201488	CDKN2B
2871896	CDO1
3396770	CDON
4024373	CDR1
3684782	CDR2
2734270	CDS1
3863669	CEACAM1
3834257	CEACAM21
3834379	CEACAM5
3834341	CEACAM5
3834379	CEACAM6
2321813	CELA2A
2321813	CELA2B
2473991	CENPA
2771654	CENPC1
2780172	CENPE
3505937	CENPJ
2859667	CENPK
2444451	CENPL
3187577	CEP110
2463864	CEP170
2463864	CEP170L
3779817	CEP192
3464622	CEP290
2389843	CEP350
3258444	CEP55
3345593	CEP57
2351632	CEPT1
2518272	CERKL
3692701	CES1
3664982	CES2
3692701	CES4
3665049	CES8
4026263	CETN2
3662417	CETP
2902844	CFB
2373336	CFH
2373406	CFH
2373336	CFHR1
2373406	CFHR1
2373406	CFHR3
2373406	CFHR4
2781736	CFI
2522616	CFLAR
3508696	CG030
3867573	CGB
3867573	CGB2
3867573	CGB5
3867573	CGB7
3867573	CGB8
3595315	CGNL1
3817501	CHAF1A

TCID	GENE_na29
3920003	CHAF1B
3483159	CHCHD2
3099089	CHCHD7
2356721	CHD1L
3609138	CHD2
3709244	CHD3
3442054	CHD4
3906160	CHD6
3660858	CHD9
2676854	CHDH
3354799	CHEK1
3479438	CHFR
3549092	CHGA
3875179	CHGB
2451593	CHI3L1
3358538	CHID1
2607568	CHL1
4006841	CHMP5
2994835	CHN2
3915569	CHODL
3468080	CHPT1
3428671	CHPT1
4018080	CHRDL1
3615791	CHRFAM7A
3359897	CHRNA10
3129026	CHRNA2
3913775	CHRNA4
3603436	CHRNA5
3615791	CHRNA7
3708663	CHRNB1
2360346	CHRNB2
2532378	CHRND
3742351	CHRNE
2532399	CHRNG
2567242	CHST10
2646125	CHST2
3802416	CHST9
2494447	CIAO1
3529877	CIDEB
3629529	CILP
2737840	CISD2
2675504	CISH
3474104	CIT
4012178	CITED1
2976768	CITED2
3205659	CKAP2
3490655	CKAP2
3371719	CKAP5
3580769	CKB
3664785	CKLF
3621351	CKMT1A
3178583	CKS2
2573641	CLASP1
2668425	CLASP2

Figure 6 continued

TCID	GENE_na29
3862108	CLC
2345023	CLCA1
2345095	CLCA3P
3378758	CLCF1
2751385	CLCN3
2320472	CLCN6
2710599	CLDN1
3497195	CLDN10
3012019	CLDN12
2657808	CLDN16
2932593	CLDN20
3007960	CLDN4
3952762	CLDN5
3743551	CLDN7
3928415	CLDN8
3868987	CLDND2
3443891	CLEC2B
3404436	CLEC2D
2620448	CLEC3B
3443183	CLEC4E
3848525	CLEC4G
3848525	CLEC4GP1
3076868	CLEC5A
3444009	CLEC7A
2787005	CLGN
2949330	CLIC1
4027769	CLIC2
3230594	CLIC3
2955638	CLIC5
2955556	CLIC5
3919278	CLIC6
3860229	CLIP3
2475407	CLIP4
2437329	CLK2
2437329	CLK2P
3577940	CLMN
3494502	CLN5
3629494	CLPX
2406420	CLSPN
2395890	CLSTN1
3168415	CLTA
2842530	CLTB
3729172	CLTC
3129065	CLU
3775808	CLUL1
2945882	CMAH
3407926	CMAS
2668021	CMTM6
2817464	CMYA5
3793760	CNDP2
2382419	CNIH4
3971219	CNKSR2
2980516	CNKSR3
3821263	CNN1

TCID	GENE_na29
3815399	CNN2
2424102	CNN3
3260265	CNNM1
3261971	CNNM2
3693673	CNOT1
3421897	CNOT2
3074362	CNOT4
2844709	CNOT6
2774565	CNOT6L
2963859	CNR1
3758157	CNTD1
3331730	CNTF
3163728	CNTLN
3411721	CNTN1
3345940	CNTN5
2607757	CNTN6
3721989	CNTNAP1
3029900	CNTNAP2
3531163	COCH
3769969	COG1
3488253	COG3
3067080	COG5
2425756	COL11A1
2961177	COL12A1
3250486	COL13A1
3181642	COL15A1
2404546	COL16A1
3762198	COL1A1
3013054	COL1A2
2889542	COL23A1
2781441	COL25A1
2642261	COL29A1
2519577	COL3A1
3924424	COL6A2
2673345	COL7A1
2633390	COL8A1
2406579	COL8A2
3892974	COL9A3
3113133	COLEC10
3518169	COMMD6
2768145	COMMD8
3369762	COMMD9
2363084	COPA
3855324	COPE
2532064	COPS7B
3761054	COPZ2
3417531	COQ10A
2775965	COQ2
3571667	COQ6
3470549	CORO1C
3751590	CORO6
3711165	COX10
3303109	COX15
2772968	COX18

TCID	GENE_na29
2451309	COX7C
2700244	CP
3106559	CP
2647109	CPA3
3716411	CPD
2750627	CPE
2719361	CPEB2
2841699	CPEB4
2842255	CPLX2
3461341	CPM
3105904	CPNE3
2695453	CPNE4
3450655	CPNE8
2524817	CPO
3158516	CPSF1
2468920	CPSF3
2315739	CPSF3L
3421446	CPSF6
3043648	CPVL
3895118	CPXM1
2377427	CR1L
2377283	CR2
3603295	CRABP1
2438458	CRABP2
2660648	CRBN
2994558	CREB5
3677795	CREBBP
2567647	CREG2
2610136	CRELD1
3950452	CRELD2
2816536	CRHBP
3554818	CRIP2
2956563	CRISP3
3720228	CRKRS
3855104	CRLF1
2759038	CRMP1
2398193	CROCC
2398193	CROCCL1
2398193	CROCCL2
3726772	CROP
3011317	CROT
3302572	CRTAC1
2616166	CRTAP
3469865	CRY1
3391149	CRYAB
2685776	CRYBG3
2418451	CRYZ
3929821	CRYZL1
3457614	CS
3444252	CSDA
3444252	CSDAP1
2406783	CSF3R
3126504	CSGALNACT1
3243908	CSGALNACT2

Figure 6 continued

TCID	GENE_na29
2880932	CSNK1A1
2880932	CSNK1A1L
3960478	CSNK1E
3629103	CSNK1G1
3629012	CSNK1G1
2826550	CSNK1G3
3894228	CSNK2A1
3894228	CSNK2A1P
2902559	CSNK2B
3101893	CSPP1
2669930	CSRNP1
3454662	CSRNP2
2450865	CSRP1
3463056	CSRP2
3901333	CST1
3901333	CST4
3335894	CST6
2638869	CSTA
3934245	CSTB
3289631	CSTF2T
3368520	CSTF3
4020137	CT47A1
4020137	CT47A10
4020137	CT47A11
4020137	CT47A2
4020137	CT47A3
4020137	CT47A4
4020137	CT47A5
4020137	CT47A6
4020137	CT47A7
4020137	CT47A8
4020137	CT47A9
4020137	CT47B1
3533499	CTAGE5
3029230	CTAGE6
2417390	CTBP2
2420467	CTBS
3665603	CTCF
2527786	CTDSP1
3458911	CTDSP2
2617276	CTDSPL
3591909	CTDSPL2
2974330	CTGF
2341663	CTH
3110317	CTHRC1
2830946	CTNNA1
3292169	CTNNA3
3219621	CTNNAL1
2618940	CTNNB1
4000839	CTPS2
3887117	CTSA
3086206	CTSB
3124537	CTSB
3385769	CTSC

TCID	GENE_na29
3358950	CTSD
3634811	CTSH
2434609	CTSK
3216671	CTSL2
2434575	CTSS
3338552	CTTN
3069470	CTTNBP2
3848644	CTXN1
3279698	CUBN
3764022	CUEDC1
3502497	CUL4A
4019900	CUL4B
3347549	CUL5
2954355	CUL7
2954355	CUL9
2907754	CUL9
3310675	CUZD1
3389745	CWF19L2
2726542	CWH43
2773434	CXCL1
2773972	CXCL11
3286602	CXCL12
2732508	CXCL13
2876608	CXCL14
3863640	CXCL17
2773434	CXCL2
2773434	CXCL3
2773947	CXCL9
2578028	CXCR4
4024420	CXorf18
4003895	CXorf21
4002011	CXorf23
3973891	CXorf27
4006504	CXorf36
3981474	CXorf50B
3986230	CXorf57
3980264	CXorf62
3807809	CXXC1
2831350	CXXC5
3709213	CYB5D1
3962530	CYB5R3
2915491	CYB5R4
3973839	CYBB
2515240	CYBRD1
3613300	CYFIP1
2837266	CYFIP2
3660213	CYLD
3157217	CYP11B1
3157217	CYP11B2
3304522	CYP17A1
3261886	CYP17A1OS
2548699	CYP1B1
2523635	CYP20A1
2903034	CYP21A2

TCID	GENE_na29
3910429	CYP24A1
3258384	CYP26A1
2559189	CYP26B1
2528093	CYP27A1
3458819	CYP27B1
3862944	CYP2A13
3862944	CYP2A6
3862944	CYP2A7
3862944	CYP2A7P1
3259019	CYP2C19
3259019	CYP2C9
2955761	CYP39A1
3063501	CYP3A4
3015040	CYP3A43
3063406	CYP3A5
3063406	CYP3A5P2
3063501	CYP3A7
3551432	CYP46A1
2335048	CYP4A11
2335048	CYP4A22
3853658	CYP4F11
3823340	CYP4F12
2334986	CYP4X1
3060994	CYP51A1
3138204	CYP7B1
2344888	CYR61
4013460	CYSLTR1
3489138	CYSLTR2
3772525	CYTH1
3837836	CYTH2
3037251	CYTH3
3940001	CYTSA
3714177	CYTSB
3927392	CYYR1
3926138	D21S2089E
3517251	DACH1
3538087	DACT1
2622121	DAG1
2673830	DALRD3
2848464	DAP
2361036	DAP3
3628832	DAPK2
2577958	DARS
4031834	DAZ1
2664760	DAZ2
4031834	DAZ2
2664760	DAZ3
4031834	DAZ3
2664760	DAZ4
4031834	DAZ4
3815834	DAZAP1
2664760	DAZL
3223157	DBC1
2888800	DBN1

Figure 6 continued

TCID	GENE_na29
2425212	DBT
2515183	DCAF17
2686023	DCBLD2
3788560	DCC
3367788	DCDC1
3367917	DCDC1
2945440	DCDC2
3367788	DCDC5
3361072	DCHS1
2790486	DCHS2
3509473	DCLK1
3465274	DCN
3440192	DCP1B
2824354	DCP2
3520934	DCT
2795819	DCTD
2559967	DCTN1
3458614	DCTN2
2881554	DCTN4
3092325	DCTN6
3683845	DCUN1D3
2726828	DCUN1D4
4018218	DCX
3824212	DDA1
2420832	DDAH1
3329649	DDB2
3050388	DDC
3153633	DDEF1IT1
2321911	DDI2
3251393	DDIT4
2969350	DDO
2901970	DDR1
2364231	DDR2
3347831	DDX10
2944068	DDX18
3250055	DDX21
3577513	DDX24
3354896	DDX25
3974838	DDX3X
3974838	DDX3Y
2829488	DDX46
3766893	DDX5
2476116	DDX50
3754736	DDX52
3203086	DDX58
2450416	DDX59
3393946	DDX6
2792800	DDX60
3358262	DEAF1
3122721	DEFA4
3122721	DEFA8P
3873091	DEFB132
2382360	DEGS1
2944068	DEK

TCID	GENE_na29
3847906	DENND1C
3118651	DENND3
3629811	DENND4A
3362263	DENND5A
3449760	DENND5B
3435490	DENR
2858592	DEPDC1B
3943101	DEPDC5
3113280	DEPDC6
3151401	DERL1
3742756	DERL2
2528476	DES
3638068	DET1
3980482	DGAT2L6
3064501	DGAT2L7
3039247	DGKB
3487095	DGKH
3074912	DGKI
2413907	DHCR24
2326496	DHDDS
2817837	DHFR
3667811	DHODH
3558118	DHRS1
3719210	DHRS11
3529237	DHRS2
2397025	DHRS3
3567187	DHRS7
3235373	DHTKD1
2763805	DHX15
3311775	DHX32
3269662	DHX32
3884922	DHX35
2549007	DHX57
3722554	DHX8
3494502	DHX9
3475511	DIABLO
3983962	DIAPH2
3577870	DICER1
2336891	DIO1
3573870	DIO2
3924674	DIP2A
3414561	DIP2B
3273251	DIP2C
3214227	DIRAS2
2417362	DIRAS3
3598613	DIS3L
2385343	DISC1
2526980	DKFZp434H1419
2731636	DKFZP564O0823
2995320	DKFZP586I1420
3860912	DKFZp761D1918
3348852	DLAT
3125116	DLC1
3489708	DLEU1

TCID	GENE_na29
3513995	DLEU2
3513995	DLEU2L
3384704	DLG2
3980643	DLG3
3708306	DLG4
3743393	DLG4
3082759	DLGAP2
3883819	DLGAP4
3565663	DLGAP5
3544346	DLST
3544346	DLSTP
2333794	DMAP1
4004044	DMD
3859761	DMKN
3159735	DMRT3
2336809	DMRTB1
3981474	DMRTC1
3981474	DMRTC1B
3060051	DMTF1
2825514	DMXL1
3624145	DMXL2
2992243	DNAH11
3040897	DNAH11
2382781	DNAH14
2849056	DNAH5
2491168	DNAH6
2491089	DNAH6
2593013	DNAH7
3690084	DNAJA2
3603247	DNAJA4
3852783	DNAJB1
2656569	DNAJB11
3629811	DNAJB14
2343289	DNAJB4
3397461	DNAJB6
3961699	DNAJB7
3018866	DNAJB9
3280902	DNAJC1
3292413	DNAJC12
2642791	DNAJC13
3457201	DNAJC14
3619650	DNAJC17
3590129	DNAJC17
2806256	DNAJC21
3367965	DNAJC24
3184940	DNAJC25
3184940	DNAJC25-GNG10
3497270	DNAJC3
2340350	DNAJC6
2847264	DNAL4
2330723	DNALI1
3644664	DNASE1L2
2678298	DNASE1L3

Figure 6 continued

TCID	GENE_na29
2602770	DNER
2600155	DNPEP
3259503	DNTT
2423597	DNTTIP2
3269939	DOCK1
2601648	DOCK10
3988435	DOCK11
2622970	DOCK3
3090512	DOCK5
3159330	DOCK8
3522398	DOCK9
3929821	DONSON
3929775	DONSON
3919860	DOPEY2
3394192	DPAGT1
2902089	DPCR1
3913483	DPH3B
2584018	DPP4
3032647	DPP6
2688166	DPPA2
2688180	DPPA4
2443120	DPT
3065546	DPY19L2
3459801	DPY19L2
3065546	DPY19L2P1
3459801	DPY19L2P1
3065546	DPY19L2P2
3459801	DPY19L2P3
3107606	DPY19L4
2547386	DPY30
2424524	DPYD
2880292	DPYSL3
3984702	DRP2
3803020	DSC1
3802980	DSC2
3802924	DSC3
3393311	DSCAML1
3812074	DSEL
3783529	DSG2
3904566	DSN1
2893794	DSP
2958325	DST
3878533	DTD1
2378937	DTL
3784208	DTNA
2638962	DTX3L
4046876	DTYMK
2636626	DULLARD
2815139	DULLARD
3592214	DUOX1
3622176	DUOX1
3592214	DUOX2
3622176	DUOX2
3622239	DUOXA1

TCID	GENE_na29
3622239	DUOXA2
2887309	DUSP1
2457261	DUSP10
3719515	DUSP14
3444958	DUSP16
2518729	DUSP19
2891241	DUSP22
2362702	DUSP23
3129731	DUSP4
3263743	DUSP5
3464860	DUSP6
3593147	DUT
2391425	DVL1
3552847	DYNC1H1
3013565	DYNC1I1
4037595	DYNC1I2
2515276	DYNC1I2
2981874	DYNLT1
4004819	DYNLT3
2376894	DYRK3
2488252	DYSF
2596386	DYTN
3625391	DYX1C1
3497195	DZIP1
3521372	DZIP1
2635263	DZIP3
2401448	E2F2
2612371	EAF1
3111695	EBAG9
2883878	EBF1
3128411	EBF2
3873923	EBF4
3294242	ECD
2400518	ECE1
2413032	ECHDC2
2358360	ECM1
3214867	ECM2
2652675	ECT2
4011096	EDA2R
2388828	EDARADD
2608801	EDEM1
2447824	EDEM3
2865390	EDIL3
3891447	EDN3
2562435	EDNRB
3483159	EEF1A1
2960903	EEF1A1
2960903	EEF1AL7
2940920	EEF1E1
3962997	EFCAB6
2554018	EFEMP1
3087438	EFHA2
2665472	EFHB
2360633	EFNA3

TCID	GENE_na29
2360633	EFNA4
2869880	EFNA5
3557408	EFS
3635776	EFTUD1
3759356	EFTUD2
2739308	EGF
3969358	EGFL6
2807195	EGFLAM
3002640	EGFR
2830861	EGR1
3291601	EGR2
2484970	EHBP1
3837431	EHD2
3326461	EHF
4031136	EIF1AY
3325052	EIF2AK2
2563654	EIF2AK3
3544387	EIF2B2
2409904	EIF2B3
2330002	EIF2C4
3903288	EIF2S2
3309215	EIF3A
2584712	EIF3E
2483544	EIF3F
3945056	EIF3L
2655688	EIF4G1
2400373	EIF4G3
3008144	EIF4H
3553607	EIF5
3788270	ELAC1
3848689	ELAVL1
4021433	ELF4
3427098	ELK3
3046197	ELMO1
3907830	ELMO2
2409310	ELOVL1
2941721	ELOVL2
2962113	ELOVL4
2781813	ELOVL6
3784727	ELP2
3091628	ELP3
2419432	ELTD1
2779543	EMCN
3865511	EML2
2478748	EML4
3575371	EML5
3679959	EMP2
3822657	EMR2
3852832	EMR3
2458338	ENAH
2382781	ENAH
2730503	ENAM
3345427	ENDOD1
3226709	ENDOG

Figure 6 continued

TCID	GENE_na29
2395490	ENO1
2386828	ENO1
2733767	ENOPH1
3795866	ENOSF1
2925953	ENPP1
2909020	ENPP4
2955673	ENPP5
3259253	ENTPD1
3230733	ENTPD2
3571667	ENTPD5
3260383	ENTPD7
3438772	EP400
3438772	EP400NL
2480383	EPAS1
2327677	EPB41
3883690	EPB41L1
2973995	EPB41L2
3797032	EPB41L3
2870964	EPB41L4A
3219788	EPB41L4B
2503109	EPB41L5
3284073	EPC1
2997907	EPDR1
2632225	EPHA3
2600689	EPHA4
2771342	EPHA5
2965206	EPHA7
2643592	EPHB1
2655845	EPHB3
3028858	EPHB6
2346625	EPHX4
3772187	EPR1
2456746	EPRS
3445908	EPS8
3841949	EPS8L1
3511698	EPSTI1
3728588	EPX
2868131	ERAP1
3720402	ERBB2
3417249	ERBB3
2597552	ERBB4
3865378	ERCC1
3836217	ERCC2
3288707	ERCC6
4012142	ERCC6L
2858752	ERCC8
3931765	ERG
3570049	ERH
3085065	ERI1
3683845	ERI2
3651509	ERI2
3303255	ERLIN1
3564790	ERO1L
2462329	ERO1LB

TCID	GENE_na29
3445768	ERP27
3217736	ERP44
2395177	ERRFI1
3053380	ERV3
3396107	ESAM
3800779	ESCO1
2856995	ESM1
2534664	ESPNL
2931763	ESR1
3568184	ESR2
3107548	ESRP1
3696226	ESRP2
2455933	ESRRG
3633794	ETFA
3868963	ETFB
3864430	ETHE1
2451870	ETNK2
3397589	ETS1
3039177	ETV1
3758510	ETV4
2709132	ETV5
3405207	ETV6
2423017	EVI5
3355733	EWSR1
3941907	EWSR1
2938196	EXOC2
3025005	EXOC4
3771336	EXOC7
2396480	EXOSC10
3485863	EXOSC8
2741768	EXOSC9
3150060	EXT1
3140037	EYA1
3887479	EYA2
2403335	EYA3
3078348	EZH2
3502437	F10
2755154	F11
2888741	F12
2816459	F2R
2863363	F2RL2
2423907	F3
2443370	F5
4027639	F8
2334740	FAAH
3979101	FAAH2
2404418	FABP3
3142381	FABP4
3517694	FABP5
3606304	FABP5
2838116	FABP6
3402571	FADS1
3333226	FADS2
3603932	FAH

TCID	GENE_na29
3644191	FAHD1
2565753	FAHD2A
2494064	FAHD2A
2565753	FAHD2B
2494064	FAHD2B
2984835	FAM103A1
3769969	FAM104A
3278813	FAM107B
3869097	FAM107B
3331926	FAM111A
3331903	FAM111B
2724094	FAM114A1
3029230	FAM115A
3029230	FAM115C
2678116	FAM116A
3948543	FAM118A
3355021	FAM118B
3418534	FAM119B
3179872	FAM120A
4009560	FAM120C
3490073	FAM124A
3189422	FAM125B
3041294	FAM126A
2594627	FAM126B
4022925	FAM127A
3991889	FAM127A
4022925	FAM127B
3991889	FAM127B
4022925	FAM127C
3991889	FAM127C
3225952	FAM129B
3077273	FAM131B
2528275	FAM134A
2849992	FAM134B
2777487	FAM13A
3247977	FAM13C
3290649	FAM13C
3360772	FAM160A2
3265432	FAM160B1
2638886	FAM162A
2369713	FAM163A
3104323	FAM164A
4051521	FAM166A
2576281	FAM166B
2825796	FAM170A
3759105	FAM171A2
2519294	FAM171B
3643347	FAM173A
2821981	FAM174A
2776088	FAM175A
2366941	FAM175A
2560625	FAM176A
3532353	FAM177A1
3260829	FAM178A

Figure 6 continued

TCID	GENE_na29
2475348	FAM179A
3534128	FAM179B
3549436	FAM181A
3649052	FAM18B
2628482	FAM19A1
3949722	FAM19A5
3768535	FAM20A
3244742	FAM21A
3244742	FAM21B
3244742	FAM21C
3244742	FAM21D
3310675	FAM24B
3764738	FAM33A
3256279	FAM35A
3256279	FAM35B2
3704376	FAM38A
3798778	FAM38B
3798829	FAM38B2
3921992	FAM3B
3070047	FAM3C
2678468	FAM3D
2658785	FAM43A
2962383	FAM46A
2353988	FAM46C
2731986	FAM47E
3509910	FAM48A
2528476	FAM48A
2541699	FAM49A
3996430	FAM50A
2757278	FAM53A
2830698	FAM53C
2634091	FAM55C
3705491	FAM57A
4026560	FAM58A
3803290	FAM59A
2368840	FAM5B
2448710	FAM5C
3449700	FAM60A
3417371	FAM62A
3082248	FAM62B
2434746	FAM63A
2358591	FAM63A
2423175	FAM69A
4019784	FAM70A
3839400	FAM71E1
2343170	FAM73A
3190893	FAM73B
3171425	FAM75A1
3171425	FAM75A2
3171425	FAM75A3
3171425	FAM75A4
3171425	FAM75A5
3171425	FAM75A6
3171425	FAM75A7

TCID	GENE_na29
3171425	FAM75C1
2820813	FAM81B
3619595	FAM82A2
3143330	FAM82B
3884892	FAM83D
3946146	FAM83F
2470470	FAM84A
3152558	FAM84B
3335338	FAM89B
3114365	FAM91A1
3114365	FAM91A2
3107151	FAM92A1
3107151	FAM92A2
3107151	FAM92A3
3589212	FAM98B
2610241	FANCD2
3607537	FANCI
3534248	FANCM
2584134	FAP
3321269	FAR1
3409605	FAR2
3497881	FARP1
2893130	FARS2
3257031	FAS
3257098	FAS
3079336	FASTK
2586227	FASTKD1
2797393	FAT1
2742581	FAT4
3862167	FBL
3948640	FBLN1
3576749	FBLN5
2500667	FBLN7
3623031	FBN1
2874371	FBN2
3656635	FBXL19
3755655	FBXL20
3518455	FBXL3
2966078	FBXL4
2761734	FBXL5
2802963	FBXL7
2552153	FBXO11
3813198	FBXO15
3129361	FBXO16
2396750	FBXO2
3473480	FBXO21
3602526	FBXO22
3602526	FBXO22OS
3368748	FBXO3
2978026	FBXO30
2531129	FBXO36
2980241	FBXO5
3943414	FBXO7
2886977	FBXW11

TCID	GENE_na29
3223605	FBXW2
3230530	FBXW5
2789957	FBXW7
3433591	FBXW8
2453036	FCAMR
3848492	FCER2
3544216	FCF1
3862188	FCGBP
2363689	FCGR2A
2363689	FCGR2B
2363689	FCGR2C
2440943	FCGR3A
2440943	FCGR3B
3838624	FCGRT
2815139	FCHO2
3381377	FCHSD2
3229338	FCN1
3229338	FCN2
2363852	FCRLA
3086206	FDFT1
3348189	FDX1
3391149	FDXACB1
3770457	FDXR
3333226	FEN1
3396593	FEZ1
2612100	FGD5
3708663	FGF11
2710895	FGF12
3523499	FGF14
2742109	FGF2
3441168	FGF23
3593408	FGF7
3480885	FGF9
2761829	FGFBP1
3132016	FGFR1
3413950	FGFR1OP2
3310041	FGFR2
2338487	FGGY
3057955	FGL2
2747961	FHDC1
3992408	FHL1
2568687	FHL2
3695541	FHOD1
3324447	FIBIN
3377964	FIBP
2727226	FIP1L1
3326826	FJX1
3721452	FKBP10
3043936	FKBP14
2472955	FKBP1B
3334339	FKBP2
3401119	FKBP4
2951567	FKBP5
3824963	FKBP8

Figure 6 continued

TCID	GENE_na29
3498315	FKSG29
3355733	FLI1
3748188	FLII
3110217	FLJ10489
4040117	FLJ12120
2738244	FLJ20184
3829638	FLJ21369
3358049	FLJ23519
3018011	FLJ23834
2369950	FLJ23867
3937967	FLJ26056
3953456	FLJ26056
2460470	FLJ30430
2617041	FLJ31715
3489708	FLJ31945
3346147	FLJ32810
3415046	FLJ33996
3301609	FLJ34077
2716246	FLJ35424
2926447	FLJ35700
2821761	FLJ35946
2485257	FLJ36848
3299782	FLJ37201
2536965	FLJ38379
2907396	FLJ38717
3903461	FLJ38773
3724591	FLJ39349
2672629	FLJ39534
2564816	FLJ40330
2565935	FLJ40330
3887165	FLJ40606
2536996	FLJ41327
3380647	FLJ42102
3380065	FLJ42258
3338192	FLJ42258
3636879	FLJ43276
3981361	FLJ44635
3673661	FLJ45121
3549989	FLJ45244
2812591	FLJ46010
3918953	FLJ46020
3097401	FLJ46365
2481379	FLJ46838
3722479	FLJ77644
4027176	FLNA
2625907	FLNB
3546924	FLRT2
3898355	FLRT3
3507282	FLT1
3838556	FLT3LG
2387711	FMN2
2510713	FMNL2
3414104	FMNL3
3454006	FMNL3

TCID	GENE_na29
2366941	FMO3
2433232	FMO5
2451693	FMOD
3994100	FMR1
2598261	FN1
2526806	FN1
3739147	FN3K
3227159	FNBP1
3489212	FNDC3A
2652410	FNDC3B
2545953	FNDC4
2405250	FNDC5
2350316	FNDC7
3343900	FOLH1
3372896	FOLH1
3343900	FOLH1B
3372896	FOLH1B
3339406	FOLR1
3544525	FOS
3836266	FOSB
2743085	FOSL1
3672609	FOXF1
3440598	FOXM1
3715642	FOXN1
2920475	FOXO3
2920475	FOXO3B
3019793	FOXP2
2342176	FPGT
2342220	FPGT
3869237	FPR1
3839910	FPR2
2732655	FRAS1
3486096	FREM2
3212008	FRMD3
3278401	FRMD4A
3621728	FRMD5
3287995	FRMPD2
3287995	FRMPD2L1
3287995	FRMPD2L2
2590715	FRZB
3022422	FSCN3
3183238	FSD1L
3815097	FSTL3
2875685	FSTL4
2791894	FSTL5
2545841	FTH1
2545841	FTHL3P
2419235	FUBP1
3656904	FUS
3837934	FUT2
3540552	FUT8
3830166	FXYD3
3830216	FXYD5
3393479	FXYD6

TCID	GENE_na29
2854327	FYB
2969886	FYN
2659887	FYTTD1
3343452	FZD4
3385509	FZD4
2596763	FZD5
3110272	FZD6
2523045	FZD7
2378068	G0S2
2745547	GAB1
3383227	GAB2
3404636	GABARAPL1
3404636	GABARAPL3
3217242	GABBR2
3916576	GABPA
2358700	GABPB2
2768056	GABRA4
2884845	GABRB2
3614634	GABRB3
4054481	GABRD
3585272	GABRG3
2964092	GABRR1
2341083	GADD45A
3816509	GADD45B
2765935	GAFA3
3575103	GALC
2401581	GALE
3593339	GALK2
3623472	GALK2
3181600	GALNT12
2511045	GALNT13
2384788	GALNT2
2585129	GALNT3
3484912	GALNT4
2511603	GALNT5
2751936	GALNT7
3401920	GALNT8
3479015	GALNT9
3363091	GALNTL4
3590853	GANC
2637112	GAP43
3402625	GAPDH
3146661	GAPDHL7
3189110	GAPVD1
3183238	GARNL1
3189714	GARNL3
3929721	GART
3323891	GAS2
3428268	GAS2L3
2444451	GAS5
3781245	GATA6
3825713	GATAD2A
3622386	GATM
2437205	GBA

Figure 6 continued

TCID	GENE_na29
2437205	GBAP
2684187	GBE1
3261544	GBF1
3228523	GBGT1
2421843	GBP1
2421883	GBP1
2421925	GBP2
2421883	GBP2
2421843	GBP3
2421925	GBP3
2421883	GBP3
2421995	GBP4
2421925	GBP4
2422035	GBP5
2345816	GBP6
2421925	GBP7
2512930	GCA
3945014	GCAT
2636062	GCET2
2688605	GCET2
3565524	GCH1
3048468	GCK
2957560	GCM1
3595441	GCOM1
3701459	GCSH
3174510	GDA
3103607	GDAP1
2430370	GDAP2
3855285	GDF1
3287789	GDF10
3824993	GDF15
3996404	GDI1
3275132	GDI2
3729014	GDPD1
3382319	GDPD5
3144934	GEM
2477980	GEMIN6
2649640	GFM1
2862716	GFM2
2558045	GFPT1
3308241	GFRA1
3127156	GFRA2
3685183	GGA2
3770663	GGA3
3044129	GGCT
3719161	GGNBP2
3939914	GGT1
3939009	GGT1
3939914	GGT2
3939009	GGT2
3939914	GGT3P
3939009	GGT3P
3939914	GGT8P
3223967	GGTA1

TCID	GENE_na29
3939914	GGTLC2
3939009	GGTLC2
3939914	GGTLC3
3939009	GGTLC3
3031556	GIMAP2
3031533	GIMAP4
3031573	GIMAP5
3079103	GIMAP6
3031517	GIMAP7
3031466	GIMAP8
3880827	GINS1
3703112	GINS2
3471005	GIT2
3656032	GIYD1
3656032	GIYD2
2923661	GJA1
2407755	GJA9
4054427	GJB4
3504213	GJB6
4015763	GLA
2668205	GLB1
2989537	GLCCI1
3197955	GLDC
3593931	GLDN
3698919	GLG1
3047660	GLI3
3422855	GLIPR1
3422826	GLIPR1L2
3197140	GLIS3
3197014	GLIS3
2749191	GLRB
3271018	GLRX3
2520291	GLS
3437500	GLT1D1
3824471	GLT25D1
2676319	GLT8D1
3468888	GLT8D2
3451246	GLT8D3
3978169	GLTSCR2
2447066	GLUL
2487478	GMCL1
2487478	GMCL1L
3914021	GMEB2
3861948	GMFG
2898597	GMNN
2528620	GMPPA
3210737	GNA14
3010439	GNAI1
3779207	GNAL
3661940	GNAO1
3210808	GNAQ
2391840	GNB1
3402874	GNB3
3184940	GNG10

TCID	GENE_na29
2417272	GNG12
3535628	GNG2
3333595	GNG3
3845944	GNG7
2948379	GNL1
2858752	GNL3L
2858752	GNL3LP
2907513	GNMT
2385197	GNPAT
2879028	GNPDA1
3564872	GNPNAT1
3468103	GNPTAB
3460127	GNS
3225224	GOLGA1
2617041	GOLGA4
3617458	GOLGA8A
3617574	GOLGA8A
3617458	GOLGA8B
3617574	GOLGA8B
3212848	GOLM1
3148871	GOLSYN
2451931	GOLT1A
2437645	GON4L
2971378	GOPC
2669888	GORASP1
4049835	GOT1L1
3707335	GP1BA
2711627	GP5
3306984	GPAM
3829174	GPATCH1
2402861	GPATCH3
3759186	GPATCH8
3063807	GPC2
4022447	GPC3
2615808	GPD1L
2511432	GPD2
2987038	GPER
2794584	GPM6A
2474681	GPN1
3191273	GPR107
2955932	GPR110
2955999	GPR110
2473784	GPR113
3094334	GPR124
2763278	GPR125
3581404	GPR132
3438061	GPR133
2386747	GPR137B
2505779	GPR148
2587790	GPR155
2651835	GPR160
2442911	GPR161
3978169	GPR173
3982612	GPR174

Figure 6 continued

TCID	GENE_na29
2417390	GPR177
3522644	GPR18
3417767	GPR182
3522662	GPR183
3445028	GPR19
3070873	GPR37
2576988	GPR39
2506570	GPR39
3994964	GPR50
3662808	GPR56
4001654	GPR64
2553262	GPR75
3387010	GPR83
2819779	GPR98
3985260	GPRASP1
3985305	GPRASP2
3405587	GPRC5A
3683377	GPRC5B
2888385	GPRIN1
2777839	GPRIN3
2674229	GPX1
3568603	GPX2
2835715	GPX3
3815538	GPX4
2336439	GPX7
2809831	GPX8
2636626	GRAMD1C
2827057	GRAMD3
3050462	GRB10
2584712	GRB14
3770743	GRB2
2469825	GREB1
2469157	GRHL1
2325358	GRHL3
2749222	GRIA2
3989448	GRIA3
4050485	GRIN1
3770422	GRIN2C
3218151	GRIN3A
3595441	GRINL1A
3071063	GRM8
3790529	GRP
2835006	GRPEL2
2772614	GRSF1
3755903	GSDMB
3445156	GSG1
3741585	GSG2
2691014	GSK3B
3187686	GSN
3903670	GSS
2738314	GSTCD
2350922	GSTM1
2350981	GSTM1
2350952	GSTM1

TCID	GENE_na29
2350922	GSTM2
2351004	GSTM2
2350981	GSTM2
2350952	GSTM2
2427208	GSTM3
2350922	GSTM4
2350981	GSTM4
2350922	GSTM5
2351004	GSTM5
3262509	GSTO1
3337168	GSTP1
2727535	GSX2
3574074	GTF2A1
2481379	GTF2A1L
2421753	GTF2B
2861183	GTF2H2
2861183	GTF2H2B
2861183	GTF2H2C
2861183	GTF2H2D
3435946	GTF2H3
2902013	GTF2H4
3008376	GTF2I
3008376	GTF2IP1
3056656	GTF2IRD2
3056656	GTF2IRD2B
3056656	GTF2IRD2P
3482888	GTF3A
2593352	GTF3C3
2954771	GTPBP2
2519480	GULP1
2787958	GYPB
2787902	GYPB
2504328	GYPC
2787958	GYPE
2787902	GYPE
3446845	GYS2
2809810	GZMA
3558375	GZMB
3558375	GZMH
2809793	GZMK
2876479	H2AFY
3250602	H2AFY2
2946714	H2BFS
3770944	H3F3B
2664395	HACL1
2473735	HADHB
3466687	HAL
3757288	HAP1
2832052	HARS
2832052	HARS2
2757621	HAUS3
3360401	HBB
2878273	HBEGF
3360441	HBG1

TCID	GENE_na29
3360441	HBG2
3018420	HBP1
2975287	HBS1L
4026956	HCFC1
3677356	HCFC1R1
3429406	HCFC2
2756309	hCG_1771830
3621728	hCG_1789710
2525852	hCG_2024410
3871459	hCG_2039146
2855963	HCN1
2907173	HCRP1
2328387	HCRTR1
2606026	HDAC4
4012204	HDAC8
2991395	HDAC9
3998444	HDHD1A
2462456	HEATR1
2386867	HEATR1
3659888	HEATR3
3559690	HEATR5A
3765059	HEATR6
3445123	HEBP1
3559570	HECTD1
3257750	HECTD2
2409970	HECTD3
2999334	HECW1
2692909	HEG1
3420497	HELB
3258910	HELLS
2776026	HELQ
3768015	HELZ
3217077	HEMGN
3628650	HERC1
3614901	HERC2
3585749	HERC2
3614901	HERC2P2
3585749	HERC2P2
3614901	HERC2P3
3585749	HERC2P3
2735459	HERC3
3292448	HERC4
2735362	HERC6
3662387	HERPUD1
2605735	HES6
3632152	HEXA
3738842	HEXDC
3774975	HEXDC
3723348	HEXIM1
2924492	HEY2
2422612	HFM1
4047070	HGD
2745899	HHIP
2457496	HHIPL2

Figure 6 continued

TCID	GENE_na29
2635184	HHLA2
3938113	HIC2
3539070	HIF1A
3836705	HIF3A
2739160	HIGD1A
3057370	HIP1
2352758	HIPK1
3075778	HIPK2
3325907	HIPK3
3952637	HIRA
3952703	HIRA
2822407	HISPPD1
3621276	HISPPD2A
2946194	HIST1H1A
2946714	HIST1H2BK
2946215	HIST1H3B
2899233	HIST1H3E
2899146	HIST1H4C
2947081	HIST1H4L
2895159	HIVEP1
2977265	HIVEP2
3250278	HK1
2948926	HLA-B
2948887	HLA-B
2948926	HLA-C
2948887	HLA-C
2950263	HLA-DMB
2950329	HLA-DPA1
2903401	HLA-DPB1
2950125	HLA-DQB2
2903189	HLA-DRA
2901620	HLA-E
3727583	HLF
3881282	HM13
3091848	HMBOX1
3602873	HMG20A
3817040	HMG20B
3431483	HMGA1
3471198	HMGA1
3420316	HMGA2
3994915	HMGB3
2329386	HMGB4
2958117	HMGCLL1
2815965	HMGCR
3944046	HMGXB4
2838656	HMMR
2841802	HMP19
3770606	HN1
3754797	HNF1B
2352609	HNRNPA3
2843619	HNRNPAB
2775463	HNRNPD
3861617	HNRNPL
4037595	HNRNPM

TCID	GENE_na29
2401275	HNRNPR
2864237	HOMER1
3448152	HOMER1
3096368	HOOK3
3042994	HOXA13
3042816	HOXA4
3761441	HOXB8
2516967	HOXD1
2516853	HOXD9
2400322	HP1BP3
2408041	HPCAL4
2794408	HPGD
3830065	HPN
3991698	HPRT1
2700244	HPS3
2647216	HPS3
3358090	HRAS
2658275	HRASLS
3867708	HRC
2656650	HRG
3145980	HRSP12
2345196	HS2ST1
4022183	HS6ST2
3671448	HSBP1
3328069	HSD17B12
3216195	HSD17B3
3417703	HSD17B6
2903488	HSD17B8
3120358	HSF1
2923819	HSF2
4025485	HSFX1
4025485	HSFX2
3400034	HSN2
3580179	HSP90AA1
3580179	HSP90AA4P
2908474	HSP90AB1
2908474	HSP90AB3P
3429312	HSP90B1
3429312	HSP90B3P
3874402	HSPA12B
3925439	HSPA13
2902707	HSPA1A
2902707	HSPA1B
2949450	HSPA1L
2828856	HSPA4
2742935	HSPA4L
3225398	HSPA5
2413519	HSPB11
2692136	HSPBAP1
2693733	HSPD1
2400793	HSPG2
3508330	HSPH1
2730194	HTN3
2401251	HTR1D

TCID	GENE_na29
2916067	HTR1E
3513147	HTR2A
2655325	HTR3C
2655325	HTR3D
2715820	HTT
3049840	HUS1
4009315	HUWE1
3471327	HVCN1
3697434	HYDIN
2977621	HYMAI
3394123	HYOU1
2539821	IAH1
2380991	IARS2
2735129	IBSP
2962525	IBTK
3038065	ICA1
3820443	ICAM1
3766621	ICAM2
3820469	ICAM5
2394588	ICMT
2401493	ID3
3300350	IDE
2597010	IDH1
3603199	IDH3A
3273601	IDI1
3095223	IDO1
3095257	IDO2
4025339	IDS
2756831	IDUA
3226883	IER5L
2362394	IFI16
2343511	IFI44
2343473	IFI44L
2403261	IFI6
3257268	IFIT5
3315675	IFITM1
3201242	IFNA10
3201242	IFNA16
3201242	IFNA17
3201242	IFNA21
3201242	IFNA4
3201242	IFNA7
3918447	IFNAR2
3201359	IFNE
2446198	IFRG15
3676002	IFT140
3480411	IFT88
3980455	IGBP1
3610804	IGF1R
2708922	IGF2BP2
3041409	IGF2BP3
2934308	IGF2R
3049292	IGFBP3
2598828	IGFBP5

Figure 6 continued

TCID	GENE_na29
3415744	IGFBP6
2770469	IGFBP7
2728448	IGFBP7
3836614	IGFL2
3375735	IGHG1
2772566	IGJ
2563785	IGK@
2563785	IGKC
2563785	IGKV1-5
2563785	IGKV3-15
2563785	IGKV3-20
2563785	IGKV3D-11
2563785	IGKV3D-15
3954764	IGLL3
4021777	IGSF1
2701109	IGSF10
3096092	IKBKB
2597867	IKZF2
3755862	IKZF3
2452948	IL10
3167553	IL11RA
3988538	IL13RA1
4018729	IL13RA2
2624565	IL17RB
3391255	IL18
2497119	IL18R1
2571569	IL1F8
2657831	IL1RAP
3972657	IL1RAPL1
2497082	IL1RL1
2497028	IL1RL2
3832906	IL28A
3832906	IL28B
3832906	IL29
3275729	IL2RA
2660617	IL5RA
2806468	IL7R
2731332	IL8
2599303	IL8RA
2599303	IL8RB
2527580	IL8RB
2599303	IL8RBP
2527580	IL8RBP
3996971	IL9R
3367965	IMMP1L
2562685	IMMT
3142485	IMPA1
3782166	IMPACT
3136413	IMPAD1
3071700	IMPDH1
2673873	IMPDH2
3262129	INA
3554315	INF2
2536757	ING5

TCID	GENE_na29
2596162	INO80D
2520113	INPP1
2495446	INPP4A
2787459	INPP4B
3267382	INPP5F
3942766	INPP5J
3740264	INPP5K
3339423	INPPL1
2502424	INSIG2
3848243	INSR
3088405	INTS10
2738314	INTS12
3383081	INTS4
3383081	INTS4L1
3383081	INTS4L2
3514488	INTS6
2742829	INTU
2950823	IP6K3
2980449	IPCEF1
3853658	IPMK
2811812	IPO11
3319840	IPO7
2604998	IQCA1
2328767	IQCC
3472274	IQCD
2713664	IQCG
3599059	IQCH
2649824	IQCJ
2816298	IQGAP2
2366028	IQWD1
2610359	IRAK2
3412296	IRAK4
2796384	IRF2
2453881	IRF6
2601995	IRS1
3525234	IRS2
4017694	IRS4
2846522	IRX2
3430776	ISCU
2438482	ISG20L2
2808931	ISL1
3621948	ISLR
2827709	ISOC1
3882854	ITCH
3690193	ITFG1
3401119	ITFG2
3642707	ITFG3
2809128	ITGA1
2356218	ITGA10
3630736	ITGA11
2809245	ITGA2
3759137	ITGA2B
3726154	ITGA3
2518272	ITGA4

TCID	GENE_na29
2515627	ITGA6
3457101	ITGA7
2617188	ITGA9
3741585	ITGAE
2519229	ITGAV
3852832	ITGB1
3284188	ITGB1
2539765	ITGB1BP1
3724545	ITGB3
2416218	ITGB3BP
2692816	ITGB5
2583465	ITGB6
2991860	ITGB8
3499132	ITGBL1
3276337	ITIH5
4009751	ITIH5L
2837232	ITK
4013549	ITM2A
3874249	ITPA
2608469	ITPR1
3448152	ITPR2
2903782	ITPR3
3918779	ITSN1
3589905	IVD
2448073	IVNS1ABP
2931172	IYD
3160895	JAK2
2880361	JAKMIP2
3916527	JAM2
3248986	JMJD1C
3291682	JMJD1C
2817291	JMY
3672886	JPH3
3157060	JRK
3556990	JUB
2415084	JUN
2945440	KAAG1
3998766	KAL1
2639734	KALRN
3850676	KANK2
3699757	KARS
2978957	KATNA1
3507962	KATNAL1
3787187	KATNAL2
2514413	KBTBD10
3389566	KBTBD3
3511168	KBTBD6
3511168	KBTBD7
2628260	KBTBD8
2427619	KCNA3
2648991	KCNAB1
3103062	KCNB2
3462567	KCNC2
3021009	KCND2

Figure 6 continued

TCID	GENE_na29
2428119	KCND3
2613293	KCNH8
2762944	KCNIP4
2603960	KCNJ13
3920850	KCNJ15
3733238	KCNJ16
3733275	KCNJ2
3931495	KCNJ6
2385873	KCNK1
2379974	KCNK2
3334446	KCNK4
2952834	KCNK5
3296046	KCNMA1
2653673	KCNMB2
3421985	KCNMB4
3824666	KCNN1
2436826	KCNN3
3317352	KCNQ1
3154002	KCNQ3
2471384	KCNS3
3071878	KCP
3470793	KCTD10
3687308	KCTD13
3383130	KCTD14
3944637	KCTD17
2594435	KCTD18
2380055	KCTD3
3128372	KCTD9
3128372	KCTD9P2
2827525	KDELC1
3867092	KDELR1
3945314	KDELR3
3817733	KDM4B
3161566	KDM4C
3439603	KDM5A
2451309	KDM5B
4009062	KDM5C
3709153	KDM6B
2769810	KDR
3593408	KGFLP1
3593408	KGFLP2
2960774	KHDC1
2959039	KHDRBS2
3117384	KHDRBS3
3847814	KHSRP
2399620	KIAA0090
3750872	KIAA0100
3629103	KIAA0101
2832963	KIAA0141
3672368	KIAA0182
2713555	KIAA0226
3542145	KIAA0247
3554452	KIAA0284
2406139	KIAA0319L

TCID	GENE_na29
3829638	KIAA0355
2973232	KIAA0408
3681956	KIAA0430
2338719	KIAA0485
2393654	KIAA0495
3193870	KIAA0649
3329404	KIAA0652
3456955	KIAA0748
3743119	KIAA0753
2331213	KIAA0754
3565739	KIAA0831
3301263	KIAA0894
2437753	KIAA0907
2748198	KIAA0922
3429754	KIAA1033
3255402	KIAA1128
3238962	KIAA1217
3884640	KIAA1219
2927604	KIAA1244
2432851	KIAA1245
3250093	KIAA1279
3737488	KIAA1303
3529951	KIAA1305
2350489	KIAA1324
3059942	KIAA1324L
3784999	KIAA1328
2689286	KIAA1407
3549264	KIAA1409
3161167	KIAA1432
3791168	KIAA1468
3075431	KIAA1549
2911257	KIAA1586
3308489	KIAA1598
3702499	KIAA1609
3737274	KIAA1618
3806126	KIAA1632
3961496	KIAA1659
2735815	KIAA1680
3854836	KIAA1683
2588319	KIAA1715
3164601	KIAA1797
2484457	KIAA1841
3258168	KIF11
3221822	KIF12
3898796	KIF16B
3734292	KIF19
2319661	KIF1B
3450775	KIF21A
3203935	KIF24
3212232	KIF27
2875419	KIF3A
3418298	KIF5A
3283991	KIF5B
2509900	KIF5C

TCID	GENE_na29
2672629	KIF9
3841756	KIR2DL1
3841777	KIR2DL1
4053056	KIR2DL1
3841756	KIR2DL2
3841777	KIR2DL2
4053056	KIR2DL2
3841756	KIR2DL3
3841777	KIR2DL3
4053056	KIR2DL3
3841777	KIR2DL4
3841756	KIR2DS1
3841777	KIR2DS1
4053056	KIR2DS1
3841756	KIR2DS2
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3841756	KIR2DS4
3841777	KIR2DS4
4053056	KIR2DS4
3841756	KIR2DS5
3841777	KIR2DS5
4053056	KIR2DS5
3841756	KIR3DL1
3841777	KIR3DL1
4053056	KIR3DL1
3841756	KIR3DL2
3841777	KIR3DL2
3841777	KIR3DL3
3841777	KIR3DP1
3841777	KIR3DP1
4053056	KIR3DP1
4053056	KIR3DP1
3841777	KIR3DS1
4053056	KIR3DS1
3841357	KIR3DX1
2727587	KIT
2724308	KLB
3553872	KLC1
3836217	KLC3
2954355	KLC4
3851840	KLF1
2723997	KLF3
3219215	KLF4
3493543	KLF5
3274361	KLF6
2596514	KLF7
3978943	KLF8
3534886	KLHDC1
2907568	KLHDC3
2452440	KLHDC8A
2622006	KLHDC8B

Figure 6 continued

TCID	GENE_na29
3721485	KLHL10
2451428	KLHL12
2750527	KLHL2
3825260	KLHL26
3562671	KLHL28
2918037	KLHL32
3983324	KLHL4
2708066	KLHL6
2776998	KLHL8
3868828	KLK10
3868841	KLK11
3868857	KLK12
3868783	KLK7
3444180	KLRA1
3443804	KLRB1
3444117	KLRC1
3444117	KLRC2
3444117	KLRC3
3444086	KLRC4
3404660	KLRD1
3404030	KLRG1
3444086	KLRK1
3272566	KNDC1
3435362	KNTC1
2691982	KPNA1
4041113	KPNA2
2703217	KPNA4
2922840	KPNA5
3724782	KPNB1
3030585	KPNB1
3447863	KRAS
3422855	KRR1
3462693	KRR1
3415576	KRT18
3757108	KRT19
3415320	KRT7
3455752	KRT77
3455890	KRT79
3455516	KRT8
3455134	KRT80
3455344	KRT82
3923838	KRTAP10-12
3923838	KRTAP10-4
3923838	KRTAP10-6
3923838	KRTAP10-7
3934623	KRTAP12-1
3934623	KRTAP12-2
3923881	KRTAP12-3
3721279	KRTAP9-2
3721279	KRTAP9-3
3721279	KRTAP9-4
3721279	KRTAP9-8
3721279	KRTAP9-9
2696415	KY

TCID	GENE_na29
2508520	KYNU
2339334	L1TD1
3797295	L3MBTL4
3597421	LACTB
3841506	LAIR1
3841357	LAIR2
3841506	LAIR2
2925237	LAMA2
3913018	LAMA5
3067302	LAMB1
2674047	LAMB2
2453793	LAMB3
3067408	LAMB4
2371065	LAMC1
2371139	LAMC2
4019849	LAMP2
2707876	LAMP3
3973768	LANCL3
2836738	LARP1
2743085	LARP2
3414512	LARP4
2740005	LARP7
4010860	LAS1L
3855285	LASS1
3454296	LASS5
2514122	LASS6
3008164	LAT2
2978989	LATS1
3504526	LATS2
3348568	LAYN
2458289	LBR
2382781	LBR
3599280	LBXCOR1
2962026	LCA5
3696035	LCAT
3653619	LCMT1
3190190	LCN2
2762500	LCORL
3512874	LCP1
2886595	LCP2
2577856	LCT
3304215	LDB1
2762088	LDB2
3446868	LDHB
2400793	LDLRAD2
4024420	LDOC1
3963289	LDOC1L
2828796	LEAP2
2649182	LEKR1
2452478	LEMD1
3420079	LEMD3
2340433	LEPR
2340433	LEPROT
3414776	LETMD1

TCID	GENE_na29
3944882	LGALS1
3833183	LGALS13
3960174	LGALS2
3536706	LGALS3
3861557	LGALS4
2462456	LGALS8
2386867	LGALS8
3258713	LGI1
3127352	LGI3
3859668	LGI4
3577078	LGMN
3367096	LGR4
3422144	LGR5
2375144	LGR6
3867573	LHB
2552368	LHCGR
2863885	LHFPL2
3224220	LHX6
2342475	LHX8
2854092	LIFR
3718401	LIG3
3841545	LILRA1
3841357	LILRA2
3841545	LILRB1
3454331	LIMA1
2725061	LIMCH1
3893642	LIME1
3008108	LIMK1
3942838	LIMK2
2574984	LIMS2
2838598	LIN28B
2775858	LIN54
3367183	LIN7C
3202528	LINGO2
3787855	LIPG
2708855	LIPH
2868265	LIX1
2356142	LIX1L
3460584	LLPH
2565484	LMAN2L
3081624	LMBR1
2660029	LMLN
2361279	LMNA
2985342	LMNA
3368814	LMO2
3446137	LMO3
2345286	LMO4
2451043	LMOD1
3008376	LOC100093631
3028011	LOC100124692
2366798	LOC100127910
3830216	LOC100127972
3442054	LOC100127974
3795184	LOC100127994

Figure 6 continued

TCID	GENE_na29
2321238	LOC100128068
3913018	LOC100128184
3777470	LOC100128219
3302056	LOC100128320
3872604	LOC100128398
3817733	LOC100128439
3836614	LOC100128529
2933175	LOC100128551
2606026	LOC100128563
3848243	LOC100128567
3890870	LOC100128608
3020222	LOC100128868
2321466	LOC100129042
3396107	LOC100129069
3765689	LOC100129112
3759587	LOC100129115
2601414	LOC100129171
2900269	LOC100129195
2404122	LOC100129196
2869880	LOC100129233
2604998	LOC100129258
2691014	LOC100129275
2587520	LOC100129312
3696317	LOC100129324
3623031	LOC100129397
2969886	LOC100129399
3050388	LOC100129427
2889916	LOC100129453
2746693	LOC100129572
3090436	LOC100129717
3128271	LOC100129717
3290746	LOC100129721
3191273	LOC100129785
3400730	LOC100129797
3092415	LOC100129846
2409904	LOC100129897
3833183	LOC100129935
2577482	LOC100129961
3737697	LOC100130078
2563785	LOC100130100
2431595	LOC100130131
3439836	LOC100130219
2504328	LOC100130248
3742351	LOC100130311
2462693	LOC100130331
2614369	LOC100130354
2774817	LOC100130356
2942306	LOC100130357
3856720	LOC100130518
3826803	LOC100130518
3542145	LOC100130542
2662581	LOC100130542
3935016	LOC100130597
3739867	LOC100130876

TCID	GENE_na29
3987029	LOC100130886
3946146	LOC100130899
2540317	LOC100130910
3275922	LOC100130920
2861952	LOC100130998
2602901	LOC100131015
2533670	LOC100131101
3110272	LOC100131102
3848243	LOC100131165
3814701	LOC100131178
2542795	LOC100131373
3754041	LOC100131384
3754096	LOC100131384
4040117	LOC100131384
4040849	LOC100131384
4025339	LOC100131434
3464860	LOC100131490
3868330	LOC100131519
3875642	LOC100131599
3227846	LOC100131612
3259367	LOC100131720
2994835	LOC100131724
3756193	LOC100131821
3754677	LOC100131822
2779638	LOC100131829
2622026	LOC100131840
4027176	LOC100131857
2984884	LOC100131869
3155937	LOC100131910
2364677	LOC100131938
3513549	LOC100131993
3681705	LOC100131998
3684782	LOC100131998
3684548	LOC100131998
2853642	LOC100132000
2824902	LOC100132014
3583541	LOC100132025
2984275	LOC100132188
4042198	LOC100132235
3650300	LOC100132247
3652077	LOC100132247
3922793	LOC100132338
3275132	LOC100132353
2431112	LOC100132495
3552729	LOC100132532
4040117	LOC100132544
2641341	LOC100132731
3392332	LOC100132764
2321466	LOC100132942
3855538	LOC100133072
3636879	LOC100133144
3017547	LOC100133169
3298924	LOC100133190
2342220	LOC100133219

TCID	GENE_na29
3735847	LOC100133227
3930781	LOC100133286
3279575	LOC100133308
3056656	LOC100133748
3309936	LOC100133773
3171425	LOC100133802
3841357	LOC100133875
3746881	LOC100133918
2565935	LOC100133923
3223425	LOC100133950
3976240	LOC100133957
3514879	LOC100134095
3759849	LOC100134130
3287366	LOC100134152
3227846	LOC100134189
3274758	LOC100134257
3754041	LOC100134348
3754096	LOC100134348
4040117	LOC100134348
4040849	LOC100134348
3050462	LOC100134631
3636879	LOC100134869
3325503	LOC100190939
3652077	LOC100190986
3279108	LOC100192204
3260001	LOC100270710
3683050	LOC100271836
3724591	LOC100272146
2993590	LOC100272146
4025339	LOC100272228
3454147	LOC100286844
2881607	LOC134466
3710681	LOC139201
3542847	LOC145474
3840857	LOC147804
2468105	LOC150622
2564816	LOC150759
2575897	LOC150776
2687739	LOC151657
2880361	LOC153469
2808180	LOC153684
3220846	LOC158402
3765167	LOC162632
3748400	LOC162632
3278234	LOC168474
3402978	LOC171220
3838809	LOC199800
2927604	LOC202451
3107606	LOC203107
3280787	LOC219688
3514879	LOC220115
3533499	LOC220429
3765167	LOC220594
3748400	LOC220594

Figure 6 continued

TCID	GENE_na29
2906607	LOC221442
3937967	LOC26080
3953456	LOC26080
3523499	LOC283480
3487095	LOC283508
3542847	LOC283567
3613338	LOC283683
3583541	LOC283767
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2571075	LOC285074
2781325	LOC285456
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2791419	LOC285505
2951567	LOC285847
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3139882	LOC286190
3650300	LOC339047
2404958	LOC339483
3205834	LOC340508
2670903	LOC348817
3686587	LOC388242
3954729	LOC388882
2472955	LOC388931
3017080	LOC389137
3212232	LOC389765
3851651	LOC389791
3704567	LOC390748
2539869	LOC392510
3826656	LOC400680
2421883	LOC400759
3960478	LOC400927
2565935	LOC400986
2576526	LOC401010
4026560	LOC401218
2994558	LOC401317
3060994	LOC401387
2988594	LOC402509
3358950	LOC402778
3244055	LOC439911
3770944	LOC440093
3583541	LOC440243
3614901	LOC440248
3585749	LOC440248
4002011	LOC440258
2593796	LOC440258
3652077	LOC440354
3683050	LOC440354
3724698	LOC440434
4040117	LOC440434
2563785	LOC440871
3173508	LOC440897
2727226	LOC441016

TCID	GENE_na29
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2995076	LOC441208
3029230	LOC441294
3641597	LOC441734
2431595	LOC51152
3948259	LOC553158
3201345	LOC554202
3819016	LOC554363
3652077	LOC595101
3683050	LOC595101
3060994	LOC613126
3652077	LOC641298
3683050	LOC641298
3938817	LOC642311
2938196	LOC642335
2506335	LOC642669
3674504	LOC643224
3405207	LOC643287
2455418	LOC643454
3281068	LOC643475
3329069	LOC644172
2506335	LOC644525
3982423	LOC644732
3982423	LOC644756
3924929	LOC645159
3583541	LOC645162
2340350	LOC645196
3583541	LOC645202
3171425	LOC645961
3283613	LOC645984
3629811	LOC646358
3203311	LOC646808
3826803	LOC646864
3621276	LOC647471
3868330	LOC647678
2525533	LOC648149
2714200	LOC649851
3621276	LOC649956
2563785	LOC650405
3939914	LOC650860
2563785	LOC652493
3642162	LOC652595
2563785	LOC652694
3692701	LOC652708
2565935	LOC652726
3841777	LOC652779
2858134	LOC653198
3937967	LOC653264
3953456	LOC653264
4015838	LOC653354
3754041	LOC653382
3754096	LOC653382
4040117	LOC653382
4040849	LOC653382

TCID	GENE_na29
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3684782	LOC653390
3684548	LOC653390
3724698	LOC653498
3754041	LOC653498
3754096	LOC653498
4040117	LOC653498
4040849	LOC653498
3206317	LOC653501
2431886	LOC653513
3591281	LOC653566
2470470	LOC653602
2575949	LOC654264
2501317	LOC654433
3358112	LOC692247
4046876	LOC727761
2628482	LOC727775
3841756	LOC727787
3841777	LOC727787
3583541	LOC727832
4026560	LOC727895
2911903	LOC727916
3635776	LOC727963
2390518	LOC728060
3504691	LOC728099
3937967	LOC728212
3953456	LOC728212
3721279	LOC728341
3029646	LOC728377
3683050	LOC728423
3471769	LOC728543
2888103	LOC728554
2487995	LOC728731
2758602	LOC728731
3223425	LOC728779
3754041	LOC728824
3754096	LOC728824
4040117	LOC728824
4040849	LOC728824
3754070	LOC728830
2431886	LOC728989
4040117	LOC729034
2619521	LOC729085
2743085	LOC729231
2565753	LOC729234
2494064	LOC729234
2500275	LOC729312
3937967	LOC729461
3953456	LOC729461
3683050	LOC729513
3652077	LOC729602
2934308	LOC729603
4002011	LOC729609
2343823	LOC729828

Figure 6 continued

TCID	GENE_na29
2548274	LOC729882
3855538	LOC729991
3855538	LOC729991-MEF2B
2936857	LOC730031
3681705	LOC730092
3684548	LOC730092
3826803	LOC730110
2758602	LOC731528
3717052	LOC731788
2390518	LOC731985
3721279	LOC732428
4031834	LOC732447
3651509	LOC81691
3248986	LOC84989
2788800	LOC90826
3954764	LOC91316
3938817	LOC96610
3847356	LONP1
3659306	LONP2
3690470	LONP2
2567167	LONRF2
3988638	LONRF3
2872848	LOX
3302693	LOXL4
3220384	LPAR1
3442137	LPAR5
2845973	LPCAT1
3661718	LPCAT2
3442427	LPCAT3
2343823	LPHN2
2728938	LPHN3
3088486	LPL
3374402	LPXN
2789266	LRBA
3488602	LRCH1
2659918	LRCH3
3336576	LRFN4
3846831	LRG1
3025291	LRGUK
2680591	LRIG1
3459120	LRIG3
2739289	LRIT3
3408505	LRMP
3528895	LRP10
2979111	LRP11
2979187	LRP11
3147985	LRP12
2578790	LRP1B
2586038	LRP2
2796847	LRP2BP
3829242	LRP3
3158812	LRRC14
2898746	LRRC16A

TCID	GENE_na29
2672190	LRRC2
3402984	LRRC23
3158812	LRRC24
2704763	LRRC34
3665458	LRRC36
3767169	LRRC37A
3767169	LRRC37A2
3767169	LRRC37A3
3767169	LRRC37A4
3717452	LRRC37B
3717452	LRRC37B2
2425173	LRRC39
2417737	LRRC40
3712835	LRRC48
3600212	LRRC49
3370269	LRRC4C
3671607	LRRC50
2365086	LRRC52
3358090	LRRC56
3358112	LRRC56
3315907	LRRC56
3154136	LRRC6
3106559	LRRC69
2341387	LRRC7
2811812	LRRC70
3190778	LRRC8A
2345880	LRRC8B
2345929	LRRC8C
3538403	LRRC9
3105430	LRRCC1
2534456	LRRFIP1
2669184	LRRFIP2
3424705	LRRIQ1
2418339	LRRIQ3
2608309	LRRN1
3019158	LRRN3
3380996	LRTOMT
2690012	LSAMP
3846831	LSDP5
3131844	LSM1
3131205	LSM12
2746269	LSM6
3317071	LSP1
3830246	LSR
3529877	LTB4R
3529877	LTB4R2
2476510	LTBP1
3571944	LTBP2
2672140	LTF
3674960	LUC7L
3465248	LUM
3324162	LUZP2
2824902	LVRN
3119339	LY6E

TCID	GENE_na29
2902559	LY6G5B
2949230	LY6G5C
3119213	LY6K
2583254	LY75
2363248	LY9
2566689	LYG2
3098977	LYN
2576988	LYPD1
2506570	LYPD1
2510056	LYPD6
2509988	LYPD6B
3135567	LYPLA1
2380785	LYPLAL1
3683845	LYRM1
2916825	LYRM2
3447863	LYRM5
2828135	LYRM7
2461999	LYST
3362826	LYVE1
3421511	LYZ
3403981	M6PR
3040518	MACC1
2331213	MACF1
2576281	MAD2L1
2396781	MAD2L2
2714672	MAEA
3905875	MAFB
3451814	MAFG
2708610	MAGEF1
3058209	MAGI2
2352609	MAGI3
3745525	MAGOH2
3444195	MAGOHB
3130823	MAK16
7385515	MALAT1
3790259	MALT1
3174121	MAMDC2
2786732	MAML3
3994710	MAMLD1
2971801	MAN1A1
2353881	MAN1A2
2326049	MAN1C1
2823551	MAN2A1
3608466	MAN2A2
3633347	MAN2C1
2779897	MANBA
3884158	MANBAL
2917767	MANEA
2330843	MANEAL
3975227	MAOA
4008210	MAOB
2814756	MAP1B
2525533	MAP2
3710681	MAP2K4

Figure 6 continued

TCID	GENE_na29
3599162	MAP2K5
3733065	MAP2K6
2574798	MAP3K2
2403027	MAP3K6
2930592	MAP3K7IP2
2672966	MAP4
2549260	MAP4K3
2496727	MAP4K4
2330289	MAP7D1
3954238	MAPK1
2776670	MAPK10
2904946	MAPK13
2904877	MAPK14
3788097	MAPK4
3111561	MAPK6
3713874	MAPK7
3329069	MAPK8IP1
2890605	MAPK9
2622912	MAPKAPK3
3784344	MAPRE2
2792166	MARCH1
2801608	MARCH6
3553690	MARK3
3260001	MARVELD1
3667652	MARVELD3
2396415	MASP2
2812690	MAST4
3240012	MASTL
2404122	MATN1
3108526	MATN2
3568667	MAX
3808600	MBD2
2694785	MBD4
3497586	MBNL2
2539607	MBOAT2
3870570	MBOAT7
3762625	MBTD1
3971329	MBTPS2
3674504	MC1R
4024092	MCF2
3924518	MCM3AP
3924518	MCM3APAS
3097152	MCM4
3063685	MCM7
3083778	MCPH1
3809592	MCTP2
2948564	MDC1
3019981	MDFIC
2485176	MDH1
2596386	MDH1B
3329343	MDK
3461164	MDM1
3421300	MDM2
2376037	MDM4

TCID	GENE_na29
2964350	MDN1
2962820	ME1
3385307	ME3
2847264	MED10
2647898	MED12L
3765689	MED13
4037595	MED13L
3473083	MED13L
3228635	MED22
2974188	MED23
3838947	MED25
3227846	MED27
3832964	MED29
3112713	MED30
3707990	MED31
3855538	MEF2B
2866225	MEF2C
2827299	MEGF10
3223551	MEGF9
2486178	MEIS1
3618333	MEIS2
3168508	MELK
2547332	MEMO1
2547332	MEMO1
3039485	MEOX2
3783788	MEP1B
2500550	MERTK
3020343	MET
3527745	METT11D1
3311342	METTL10
3191074	METTL11A
3375999	METTL12
3556418	METTL3
3796244	METTL4
3414739	METTL7A
3416895	METTL7B
3651955	METTL9
3808096	MEX3C
3845296	MEX3D
3748798	MFAP4
3638204	MFGE8
2653932	MFN1
3735623	MFSD11
2331679	MFSD2
2376548	MFSD4
2520138	MFSD6
2714200	MFSD7
2785035	MFSD8
3028011	MGAM
2890859	MGAT1
3534866	MGAT2
3226883	MGAT2
2566414	MGAT4A
2890239	MGAT4B

TCID	GENE_na29
3464417	MGAT4C
2668425	MGC12488
4022690	MGC16121
3705135	MGC16385
2658275	MGC2889
2877893	MGC29506
3528172	MGC40069
3011838	MGC87042
3304012	MGEA5
3445741	MGP
3646277	MGRN1
3406589	MGST1
4042837	MIA3
3320717	MICAL2
3320819	MICALCL
3999395	MID1
2885776	MINA
3742351	MINK1
3950846	MIOX
3496366	MIRHG1
3707759	MIS12
2628785	MITF
2383118	MIXL1
3312490	MKI67
3961496	MKL1
3649052	MKL2
3076178	MKRN1
3282463	MKX
3434525	MLEC
2649609	MLF1
2796510	MLF1IP
2616932	MLH1
3572235	MLH3
2734784	MLL
3847703	MLL
3453592	MLL2
3924929	MLL3
3017547	MLL5
3847703	MLLT1
3238231	MLLT10
2358693	MLLT11
3200982	MLLT3
2936857	MLLT4
3721886	MLX
2746164	MMAA
2334350	MMACHC
3763270	MMD
3388807	MMP1
3388893	MMP13
3528864	MMP14
3143643	MMP16
3143660	MMP16
3883236	MMP24
3753760	MMP28

Figure 6 continued

TCID	GENE_na29
2735759	MMRN1
3298924	MMRN2
3302360	MMS19
2748163	MND1
2362333	MNDA
3625761	MNS1
3202316	MOBKL2B
3784783	MOCOS
3064501	MOGAT3
2674963	MON1A
3919952	MORC3
4017212	MORC4
2794180	MORF4
2794180	MORF4L1
3475295	MORN3
2381309	MOSC1
4022833	MOSPD1
3708874	MPDU1
3198974	MPDZ
3480013	MPHOSPH8
3476012	MPHOSPH9
2333107	MPL
2594987	MPP4
3541073	MPP5
2993206	MPP6
3282601	MPP7
3799167	MPPE1
3367673	MPPED2
3712363	MPRIP
2545653	MPV17
3393720	MPZL2
2370317	MR1
2915571	MRAP2
2598496	MREG
3807965	MRO
3480681	MRP63
3760945	MRPL10
2955025	MRPL14
3361116	MRPL17
3379708	MRPL21
3619479	MRPL42P5
3218067	MRPL50
2664099	MRPS25
2861952	MRPS27
2808612	MRPS30
3510925	MRPS31
3409330	MRPS35
3734760	MRPS7
3188050	MRRF
2898452	MRS2
3332403	MS4A1
3374934	MS4A4E
3374934	MS4A6A
2480992	MSH2

TCID	GENE_na29
2817837	MSH3
2902633	MSH5
2696764	MSL2
3979659	MSN
3125571	MSR1
2674602	MST1
2835662	MST150
3992408	MST159
2674602	MSTP2
2674602	MSTP9
3662106	MT1A
3662106	MT1DP
3662139	MT1E
3662201	MT1F
3692999	MT1G
3662201	MT1H
3662236	MT1IP
3662139	MT1JP
3662130	MT1L
3662150	MT1M
3662201	MT1P2
3662150	MT1P3
3662106	MT1X
3662247	MT1X
3662236	MT1X
3662106	MT2A
2952102	MTCH1
3060917	MTERF
2607020	MTERFD2
3629378	MTFMT
3101385	MTFR1
3540007	MTHFD1
2931391	MTHFD1L
2731417	MTHFD2L
3482888	MTIF3
3994795	MTM1
3994846	MTMR1
3615985	MTMR10
2434178	MTMR11
3615985	MTMR15
3764471	MTMR4
3511189	MTRF1
3151970	MTSS1
3125915	MTUS1
2437118	MUC1
3366903	MUC15
3986168	MUM1L1
2676454	MUSTN1
3259019	MUTYH
3655723	MVP
3997825	MXRA5
2512701	MXRA7
3841076	MYADM
2547751	MYADML

TCID	GENE_na29
3428596	MYBPC1
3372129	MYBPC3
2407755	MYCBP
3518496	MYCBP2
2470838	MYCN
2931970	MYCT1
3622934	MYEF2
3593014	MYEF2
3338060	MYEOV
3745351	MYH1
3744463	MYH10
3682028	MYH11
3839206	MYH14
3745429	MYH2
3745351	MYH2
3745429	MYH3
3745429	MYH4
3745351	MYH4
3557504	MYH6
3557504	MYH7
3745429	MYH8
3745351	MYH8
3959451	MYH9
2597389	MYL1
2714200	MYL5
2651671	MYNN
2850071	MYO10
2520429	MYO1B
3752709	MYO1D
3626826	MYO1E
3431071	MYO1H
3624607	MYO5A
3807595	MYO5B
2914070	MYO6
3631794	MYO9A
2443952	MYOC
3300597	MYOF
3796428	MYOM1
2835619	MYOZ3
3725779	MYST2
3133135	MYST3
2724585	N4BP2
3508696	N4BP2L2
2773872	NAAA
3344142	NAALAD2
2653114	NAALADL2
2520225	NAB1
3417809	NAB2
3695268	NAE1
3074912	NAG20
2861616	NAIP
3066818	NAMPT
4012511	NAP1L2
4014759	NAP1L3

Figure 6 continued

TCID	GENE_na29
3359469	NAP1L4
2777447	NAP1L5
3901191	NAPB
3778823	NAPG
3868400	NAPSA
3868400	NAPSB
3486883	NARG1L
3627363	NARG2
3809671	NARS
2334404	NASP
4006210	NAT13
3878934	NAT5
3323052	NAV2
2541230	NBAS
3485292	NBEA
2506335	NBEA
2523478	NBEAL1
2621122	NBEAL2
2752085	NBLA00301
2432851	NBPF1
2357217	NBPF1
2432851	NBPF10
2357217	NBPF10
2432851	NBPF11
2357217	NBPF11
2432851	NBPF12
2357217	NBPF12
2432851	NBPF14
2357217	NBPF14
2432851	NBPF15
2357217	NBPF15
2432851	NBPF16
2357217	NBPF16
2432851	NBPF20
2357217	NBPF20
2432851	NBPF8
2357217	NBPF8
2432851	NBPF9
2357217	NBPF9
3147173	NCALD
3349293	NCAM1
3915936	NCAM2
3402571	NCAPD2
2762500	NCAPG
3181302	NCBP1
2713074	NCBP2
2590736	NCKAP1
2673648	NCKIPSD
2473149	NCOA1
3139722	NCOA2
3887635	NCOA3
3903525	NCOA6
2924514	NCOA7
3746881	NCOR1

TCID	GENE_na29
3839880	NCRNA00085
3656635	NCRNA00095
2762944	NCRNA00099
4028207	NCRNA00105
2390976	NCRNA00115
3879372	NCRNA00153
2363084	NCSTN
4037595	ND1
3776139	NDC80
3495076	NDFIP2
3615556	NDNL2
3555736	NDRG2
3294816	NDST2
3825838	NDUFA13
3458400	NDUFA4L2
2965674	NDUFAF4
3341497	NDUFC2
2363525	NDUFS2
2331178	NDUFS5
3778207	NDUFV2
3922921	NDUFV3
2581000	NEB
2510485	NEB
3106479	NECAB1
3625539	NEDD4
3789947	NEDD4L
3128271	NEFL
3090436	NEFM
2418078	NEGR1
3086181	NEIL2
2666884	NEK10
2642441	NEK11
3715809	NEK8
3451814	NELL2
2379068	NENF
2949471	NEU1
2343231	NEXN
3717052	NF1
3696666	NFAT5
3795184	NFATC1
3666033	NFATC3
3456666	NFE2
2588827	NFE2L2
3724591	NFE2L3
2993590	NFE2L3
2338719	NFIA
3199207	NFIB
3214451	NFIL3
3561039	NFKBIA
2634091	NFKBIZ
3904189	NFS1
2558118	NFU1
3166880	NFX1
2906607	NFYA

TCID	GENE_na29
2332013	NFYC
3529156	NGDN
3985534	NGFRAP1
2666566	NGLY1
2780060	NHEDC1
2780099	NHEDC2
2363128	NHLH1
3265047	NHLRC2
2674526	NICN1
2462160	NID1
3564620	NID2
3693083	NIP30
3613338	NIPA1
3613300	NIPA2
3146012	NIPAL2
2325410	NIPAL3
2806799	NIPBL
3956909	NIPSNAP1
3182957	NIPSNAP3A
3182957	NIPSNAP3B
3218528	NIPSNAP3B
2623859	NISCH
2363389	NIT1
2924081	NKAIN2
2549092	NKAP
2666103	NKIRAS1
2619344	NKTR
3980835	NLGN3
3715368	NLK
2812359	NLN
3662444	NLRC5
3319018	NLRP14
3636985	NMB
2877231	NME5
2673136	NME6
2447324	NMNAT2
2697902	NMNAT3
3723264	NMT1
3279108	NMT2
2770039	NMU
2882325	NMUR2
2576526	NOC2L
3439013	NOC4L
3044072	NOD1
3803628	NOL4
2942504	NOL7
3214749	NOL8
3261492	NOLC1
3649320	NOMO1
3649320	NOMO2
3649320	NOMO3
3980887	NONO
2758076	NOP14
3442024	NOP2

Figure 6 continued

TCID	GENE_na29
2364016	NOS1AP
2514216	NOSTRIN
2431112	NOTCH2
2431112	NOTCH2NL
2949901	NOTCH4
3113202	NOV
3558745	NOVA1
4015481	NOX1
3385951	NOX4
3527514	NP
3347658	NPAT
3801411	NPC1
3801411	NPC1
3571904	NPC2
3230697	NPDC1
3891006	NPEPL1
3724698	NPEPPS
4040117	NPEPPS
2695648	NPHP3
3650300	NPIP
3652077	NPIP
3652077	NPIPL1
3652077	NPIPL3
2370926	NPL
3774029	NPLOC4
3404436	NPM1
3089049	NPM2
2738378	NPNT
2359780	NPR1
2805635	NPR3
2792127	NPY1R
3696666	NQO1
3756046	NR1D1
2614142	NR1D2
3855596	NR2C2AP
3610110	NR2F2
2879312	NR3C1
3415229	NR4A1
3181976	NR4A3
3225096	NR6A1
3067478	NRCAM
3023565	NRF1
3925639	NRIP1
2940145	NRN1
3284302	NRP1
2524301	NRP2
2898371	NRSN1
2552643	NRXN1
3545634	NRXN3
3088048	NSAP11
2842951	NSD1
3724197	NSF
3894637	NSFL1C
2847292	NSUN2

TCID	GENE_na29
2334706	NSUN4
3280224	NSUN6
2724853	NSUN7
3045004	NT5C3
3757399	NT5C3L
2915828	NT5E
3143330	NTAN1
3356539	NTM
3466556	NTN4
2361761	NTRK1
3177111	NTRK2
3637818	NTRK3
2452405	NUAK2
3644162	NUBP2
3531355	NUBPL
3322251	NUCB2
2510713	NUDC
3148796	NUDCD1
4008427	NUDT10
4008427	NUDT11
3681485	NUDT14
2642543	NUDT16P
2432647	NUDT17
2951087	NUDT3
2355615	NUDT4
3235461	NUDT5
2742109	NUDT6
2364438	NUF2
3512449	NUFIP1
3571347	NUMB
2943808	NUP153
4017281	NUP62CL
3662265	NUP93
3359910	NUP98
3654699	NUPR1
2923060	NUS1
3590388	NUSAP1
3665857	NUTF2
3376155	NXF1
3739867	NXN
3305017	OBFC1
3417485	OBFC2B
2383999	OBSCN
2600237	OBSL1
3614774	OCA2
2768654	OCIAD2
2375338	OCR1
2730281	ODAM
2421121	ODF2L
4020655	ODZ1
3662041	OGFOD1
3214800	OGN
3981120	OGT
2587618	OLA1

TCID	GENE_na29
3490892	OLFM4
3319119	OLFML1
3444043	OLR1
2658346	OPA1
3301782	OPALIN
3399004	OPCML
3181976	OPHN1
2932219	OPRM1
3353914	OR10D1P
3353876	OR10G4
3353876	OR10G7
3353876	OR10G8
3353876	OR10G9
2465806	OR14A16
3188186	OR1Q1
2390180	OR2AJ1
2900832	OR2H1
2465890	OR2T12
4045946	OR2T3
2465890	OR2T33
4045946	OR2T34
2465890	OR2T8
2390180	OR2W3
3706617	OR3A4
3329983	OR4B1
3332008	OR4D6
2487995	OR7E5P
2487995	OR7E91P
3380065	ORAOV1
2594569	ORC2L
2580304	ORC4L
3658925	ORC6L
2591942	ORMDL1
3416977	ORMDL2
3418436	OS9
2693217	OSBPL11
3801621	OSBPL1A
3041875	OSBPL3
2517588	OSBPL6
3555461	OSGEP
2807359	OSMR
2542420	OSR1
2968144	OSTM1
2758602	OTOP1
2788195	OTUD4
2434233	OTUD7B
2485112	OTX1
3566176	OTX2
2331511	OXCT2
2408095	OXCT2
2612625	OXNAD1
3452664	P11
2701071	P2RY13
3513514	P2RY5

Figure 6 continued

TCID	GENE_na29
3294159	P4HA1
2875193	P4HA2
4041342	P4HB
2935311	PACRG
2720732	PACRGL
3861978	PAF1
2831209	PAIP2
2659577	PAK2
3987228	PAK3
3184408	PALM2
3184408	PALM2-AKAP2
2822215	PAM
3457696	PAN2
3483159	PAN3
3874533	PANK2
3950602	PANX2
3543539	PAPLN
2484305	PAPOLG
2780999	PAPSS1
3256590	PAPSS2
2774817	PAQR3
2438016	PAQR6
2983142	PARK2
3441011	PARP11
2639054	PARP14
3527418	PARP2
3505781	PARP4
2808748	PARP8
2692060	PARP9
2811145	PART1
3320865	PARVA
3374746	PATL1
2571608	PAX8
3532793	PAX9
2976417	PBOV1
2364677	PBX1
3855818	PBX4
2829589	PCBD2
2675801	PCBP4
2696802	PCCB
2743600	PCDH10
2878987	PCDH12
3516228	PCDH20
2722823	PCDH7
3516639	PCDH9
2832423	PCDHB10
2832431	PCDHB11
2832439	PCDHB12
2832392	PCDHB13
2832447	PCDHB13
2832325	PCDHB14
2832459	PCDHB14
2832297	PCDHB14
2832392	PCDHB16

TCID	GENE_na29
2832467	PCDHB18
2832325	PCDHB19P
2832310	PCDHB2
2832447	PCDHB2
2832297	PCDHB2
2832310	PCDHB3
2832447	PCDHB3
2832297	PCDHB3
2832315	PCDHB4
2832325	PCDHB5
2832355	PCDHB6
2832325	PCDHB9
2832533	PCDHGA1
2832533	PCDHGA10
2832533	PCDHGA11
2832533	PCDHGA12
2832533	PCDHGA2
2832533	PCDHGA3
2832533	PCDHGA4
2832533	PCDHGA5
2832533	PCDHGA6
2832533	PCDHGA7
2832533	PCDHGA8
2832533	PCDHGA9
2832533	PCDHGB1
2832533	PCDHGB2
2832533	PCDHGB3
2832533	PCDHGB4
2832533	PCDHGB5
2832533	PCDHGB6
2832533	PCDHGB7
2832533	PCDHGB8P
2832533	PCDHGC3
2832533	PCDHGC4
2832533	PCDHGC5
3342525	PCF11
2560195	PCGF1
2714230	PCGF3
3867165	PCIF1
3059258	PCLO
3059226	PCLO
3087813	PCM1
2930863	PCMT1
3134922	PCMTD1
3542689	PCNX
2461037	PCNXL2
2698996	PCOLCE2
3921599	PCP4
2868044	PCSK1
4007550	PCSK1N
3877892	PCSK2
3642200	PCSK6
3976124	PCTK1
3466826	PCTK2

TCID	GENE_na29
2712754	PCYT1A
3263944	PDCD4
2616317	PDCD6IP
3358361	PDDC1
2984275	PDE10A
2589017	PDE11A
2590582	PDE1A
3416651	PDE1B
3044597	PDE1C
3381150	PDE2A
2340529	PDE4B
2858134	PDE4D
2431886	PDE4DIP
2783596	PDE5A
2714132	PDE6B
3138464	PDE7A
3606034	PDE8A
2816681	PDE8B
3922793	PDE9A
2791197	PDGFC
3389077	PDGFD
2727226	PDGFRA
3087703	PDGFRL
3970833	PDHA1
3369249	PDHX
2639225	PDIA5
2469529	PDIA6
2540317	PDIA6
3062082	PDK4
3301218	PDLIM1
2796951	PDLIM3
2828441	PDLIM4
2736322	PDLIM5
2766568	PDS5A
3484768	PDS5B
3650300	PDXDC2
3923257	PDXK
4011637	PDZD11
2411173	PDZK1IP1
3411810	PDZRN4
3127610	PEBP4
3766796	PECAM1
2939593	PECI
2598496	PECR
3013255	PEG10
3872053	PEG3
2556302	PELI1
3537164	PELI2
2809128	PELO
2605749	PER2
2976360	PERP
3061191	PEX1
3753690	PEX12
2440117	PEX19

Figure 6 continued

TCID	GENE_na29
2465551	PEX5
2707045	PEX5L
3709540	PFAS
2440612	PFDN2
4009811	PFKFB1
2377094	PFKFB2
3233605	PFKFB3
3413344	PFKM
2700585	PFN2
3332780	PGA3
3332780	PGA4
3332780	PGA5
2593407	PGAP1
2390518	PGBD2
3288707	PGBD3
3108226	PGCP
2871685	PGGT1B
2339786	PGM1
3381925	PGM2L1
3173508	PGM5
3173508	PGM5P1
3173508	PGM5P2
3824963	PGPEP1
3988740	PGRMC1
2928930	PHACTR2
3891530	PHACTR3
3403981	PHC1
3403981	PHC1B
2405469	PHC2
2704894	PHC3
3971451	PHEX
2903673	PHF1
2986084	PHF10
3489481	PHF11
3751184	PHF12
2990043	PHF14
2829337	PHF15
3975893	PHF16
2743315	PHF17
3116535	PHF20L1
2911944	PHF3
3991650	PHF6
4009506	PHF8
4012299	PHKA1
3659156	PHKB
3359461	PHLDA2
2635906	PHLDB2
3791482	PHLPP
2428699	PHTF1
3278198	PHYH
3190796	PHYHD1
3127385	PHYHIP
3247977	PHYHIPL
3290649	PHYHIPL

TCID	GENE_na29
2905296	PI16
3259978	PI4K2A
2721777	PI4K2B
3953724	PI4KA
3953724	PI4KAP1
3953724	PI4KAP2
3589280	PIAS1
2432647	PIAS3
3493448	PIBF1
3945180	PICK1
2602653	PID1
3428268	PIGA
4000512	PIGA
2551690	PIGF
2714025	PIGG
3569339	PIGH
2418929	PIGK
3811086	PIGN
3391214	PIH1D2
3364759	PIK3C2A
2697564	PIK3CB
2395890	PIK3CD
3018309	PIK3CG
2813060	PIK3R1
2410470	PIK3R3
2525272	PIKFYVE
3015442	PILRB
3621728	PIN4
2400212	PINK1
3281068	PIP4K2A
3418303	PIP4K2C
3300869	PIP5K1A
3300869	PIPSL
3957938	PISD
3732230	PITPNC1
3437801	PIWIL1
3049700	PKD1L1
3697933	PKD1L3
2735221	PKD2
3111561	PKHD1L1
3104260	PKIA
3631964	PKM2
3822723	PKN1
3922975	PKNOX1
3354535	PKNOX2
3450234	PKP2
2511820	PKP4
3681488	PLA2G10
3376529	PLA2G16
3960388	PLA2G6
2955827	PLA2G7
2583374	PLA2R1
3136178	PLAG1
2977621	PLAGL1

TCID	GENE_na29
3133233	PLAT
3252036	PLAU
3294959	PLAU
2475042	PLB1
3875642	PLCB1
3334372	PLCB3
3875908	PLCB4
3759587	PLCD3
2527895	PLCD4
3258477	PLCE1
2316605	PLCH2
2521574	PLCL1
2612813	PLCL2
3833443	PLD3
3157901	PLEC1
2486811	PLEK
3569257	PLEK2
3268274	PLEKHA1
2517737	PLEKHA3
3867458	PLEKHA4
3407096	PLEKHA5
3451988	PLEKHA6
2995189	PLEKHA6
3451988	PLEKHA9
2995189	PLEKHA9
2505957	PLEKHB2
3107828	PLEKHF2
3832992	PLEKHG2
2798475	PLEKHG4B
3569339	PLEKHH1
2479433	PLEKHH2
3759849	PLEKHM1
3759849	PLEKHM1P
3598165	PLEKHO2
2492659	PLG
2492659	PLGLA
2492659	PLGLB1
2492659	PLGLB2
3638546	PLIN
2527196	PLK1
2858023	PLK2
2923270	PLN
2699564	PLOD2
3977067	PLP2
2645906	PLS1
3987996	PLS3
2699623	PLSCR4
3907524	PLTP
3854417	PLVAP
3755510	PLXDC1
3073267	PLXNA4
2673181	PLXNB1
3426502	PLXNC1
3911217	PMEPA1

Figure 6 continued

TCID	GENE_na29
3698081	PMFBP1
3962000	PMM1
3647504	PMM2
2988459	PMS2L3
3009580	PMS2L3
2934191	PNLDC1
3571642	PNMA1
3128731	PNMA2
3316287	PNPLA2
3067592	PNPLA8
4042198	PNRC2
2336650	PODN
3073013	PODXL
2365496	POGK
3972093	POLA1
3750625	POLDIP2
3583395	POLE2
2489606	POLE4
3607537	POLG
3766861	POLG2
3788833	POLI
2757621	POLN
2562605	POLR1A
2728448	POLR2B
2655773	POLR2H
3065154	POLR2J
3065154	POLR2J2
3065154	POLR2J3
3009838	POLR2J4
3065154	POLR2J4
3109191	POLR2K
3296512	POLR3A
3430129	POLR3B
2432647	POLR3C
2432571	POLR3GL
2988459	POM121
3057755	POM121
3009580	POM121
3057755	POM121C
2334602	POMGNT1
3057755	POMZP3
3061942	PON1
3061997	PON2
3061964	PON3
2690956	POPDC2
2967276	POPDC3
3009229	POR
3976639	PORCN
2365675	POU2F1
3352438	POU2F3
2780522	PPA2
2857204	PPAP2A
2414366	PPAP2B
3160727	PPAPDC2

TCID	GENE_na29
3192033	PPAPDC3
2763550	PPARGC1A
2773358	PPBP
2773407	PPBPL2
3338453	PPFIA1
3463821	PPFIA2
3409211	PPFIBP1
3319137	PPFIBP2
2357217	PPIAL4A
2357217	PPIAL4B
2357217	PPIAL4C
2357217	PPIAL4G
3628994	PPIB
2873105	PPIC
2514441	PPIG
3938244	PPIL2
2978989	PPIL4
3678462	PPL
3538555	PPM1A
3954294	PPM1F
2623568	PPM1M
3107342	PPM2C
2475209	PPP1CB
3471374	PPP1CC
2948425	PPP1R10
3463571	PPP1R12A
3580876	PPP1R13B
3865344	PPP1R13L
2931090	PPP1R14C
3838004	PPP1R15A
3884830	PPP1R16B
3416651	PPP1R1A
3720322	PPP1R1B
2518488	PPP1R1C
3068688	PPP1R3A
2880051	PPP2R2B
2759205	PPP2R2C
3271687	PPP2R2D
2643901	PPP2R3A
3532353	PPP2R3C
3552729	PPP2R5C
3567984	PPP2R5E
2779638	PPP3CA
3294499	PPP3CB
3798291	PPP4R1
3836760	PPP5C
3471300	PPTC7
3814701	PQLC1
4007765	PRAF2
2321058	PRAMEF1
2321058	PRAMEF13
2321058	PRAMEF14
2321058	PRAMEF2
3444578	PRB1

TCID	GENE_na29
3444578	PRB3
3444578	PRB4
3639031	PRC1
3384270	PRCP
2919669	PRDM1
3933243	PRDM15
2316953	PRDM16
2321238	PRDM2
3470037	PRDM4
3851776	PRDX2
3483885	PRDX2
2367743	PRDX6
2474265	PREB
4053085	PRELP
2550959	PREPL
3102096	PREX2
3451375	PRICKLE1
4007865	PRICKLE3
3238962	PRINS
2337716	PRKAA2
3434142	PRKAB1
2433209	PRKAB2
3852529	PRKACA
2344393	PRKACB
3453556	PRKAG1
3732885	PRKAR1A
3018375	PRKAR2B
3653123	PRKCB
2624291	PRKCD
2480168	PRKCE
3538893	PRKCH
2651916	PRKCI
3275922	PRKCQ
4054481	PRKCZ
3559192	PRKD1
2548500	PRKD3
3134034	PRKDC
3246888	PRKG1
2775214	PRKG2
3009580	PRKRIP1
3997946	PRKX
3997946	PRKY
3838809	PRMT1
3924783	PRMT2
3323443	PRMT3
2349848	PRMT6
2459173	PRO2012
3883207	PROCR
2682271	PROK2
2486851	PROKR1
2761842	PROM1
2685304	PROS1
2379665	PROX1
2358171	PRPF3

Figure 6 continued

TCID	GENE_na29
2336383	PRPF38A
3534201	PRPF39
3221543	PRPF4
3414104	PRPF40B
3454006	PRPF40B
2892738	PRPF4B
3413852	PRPH
3986514	PRPS1
3986514	PRPS1L1
3771513	PRPSAP1
3838624	PRR12
3656318	PRR14
2994981	PRR15
2984543	PRR18
3948259	PRR5
3973692	PRRG1
2662473	PRRT3
2366798	PRRX1
3028766	PRSS1
2899808	PRSS16
3028766	PRSS2
3343452	PRSS23
3028766	PRSS3
3281703	PRTFDC1
2358623	PRUNE
3210616	PRUNE2
3210497	PRUNE2
4036437	PRY
4036437	PRY2
3293762	PSAP
3175971	PSAT1
3126368	PSD3
3126191	PSD3
2501238	PSD4
3543481	PSEN1
3863929	PSG1
3863761	PSG1
3863929	PSG11
3863929	PSG2
3863761	PSG2
3863761	PSG3
3863929	PSG4
3863761	PSG4
3863929	PSG5
3863761	PSG5
3863929	PSG6
3863761	PSG6
3863929	PSG7
3863761	PSG7
3863929	PSG8
3863761	PSG8
3863929	PSG9
3863761	PSG9
3881282	PSIMCT-1

TCID	GENE_na29
3960478	psiTPTE22
3935902	psiTPTE22
3363979	PSMA1
3912861	PSMA7
2358906	PSMB4
2903285	PSMB9
3372209	PSMC3
3721886	PSMC3IP
3833291	PSMC4
3730941	PSMC5
3315549	PSMD13
2512701	PSMD14
2655650	PSMD2
3300869	PSMD4
3832383	PSMD8
3722152	PSME3
3873389	PSMF1
3035408	PSMG3
2348060	PTBP2
3014742	PTCD1
3215851	PTCH1
3727787	PTEN
3727787	PTENP1
3236786	PTER
3535752	PTGDR
2353717	PTGFRN
3220873	PTGR1
2448382	PTGS2
3156307	PTK2
2907671	PTK7
3405207	PTMA
3402736	PTMS
3074857	PTN
3839006	PTOV1
2911903	PTP4A1
2404819	PTP4A2
3118818	PTP4A3
3180142	PTPDC1
3279982	PTPLA
3164601	PTPLAD2
2692411	PTPLB
3329886	PTPMT1
3888721	PTPN1
3009959	PTPN12
2734629	PTPN13
2455418	PTPN14
2505529	PTPN18
2428796	PTPN22
2621333	PTPN23
3219885	PTPN3
3874023	PTPRA
2373842	PTPRC
3270270	PTPRE
2333318	PTPRF

TCID	GENE_na29
2626802	PTPRG
3329983	PTPRJ
2973376	PTPRK
3777470	PTPRM
2600089	PTPRN
2327817	PTPRU
3757917	PTRF
2838201	PTTG1
2838201	PTTG2
2404254	PUM1
2542816	PUM2
2831567	PURA
2315739	PUSL1
3015442	PVRIG
3394488	PVRL1
2688499	PVRL2
2635641	PVRL3
3134922	PXDNL
2626167	PXK
3880767	PYGB
3564210	PYGL
3625440	PYGO1
2362351	PYHIN1
3302740	PYROXD2
3443464	PZP
3443348	PZP
2762334	QDPR
2477438	QPCT
3325768	QSER1
2369950	QSOX1
3638204	QTRT1
3820727	QTRT1
3458451	R3HDM2
3598482	RAB11A
3131741	RAB11FIP1
3642875	RAB11FIP3
3223872	RAB14
3568616	RAB15
3890870	RAB22A
2958670	RAB23
2361257	RAB25
3625271	RAB27A
3788976	RAB27B
3384321	RAB30
2929699	RAB32
3751002	RAB34
2810805	RAB3C
2456849	RAB3GAP2
3421706	RAB3IP
2905196	RAB44
2641263	RAB7A
3707642	RABEP1
3686750	RABEP2
3188299	RABGAP1

Figure 6 continued

TCID	GENE_na29
2367963	RABGAP1L
2342624	RABGGTB
2989050	RAC1
3451960	RACGAP1
3454223	RACGAP1
3451960	RACGAP1P
3454223	RACGAP1P
2852989	RAD1
2662020	RAD18
3183757	RAD23B
2828564	RAD50
3590086	RAD51
3728776	RAD51C
3439836	RAD52
3036476	RADIL
2930957	RAET1G
2979187	RAET1G
2930957	RAET1L
2979187	RAET1L
2663244	RAF1
3327143	RAG1
2360700	RAG1AP1
3369931	RAG2
3580234	RAGE
3712675	RAI1
4001223	RAI2
2503200	RALB
3228523	RALGDS
3105271	RALYL
3438027	RAN
2499158	RANBP2
3847536	RANBP3
2853426	RANBP3L
2942504	RANBP9
2351872	RAP1A
2663244	RAP1A
2400655	rap1GAP
2736853	RAP1GDS1
3497659	RAP2A
4022032	RAP2C
2749699	RAPGEF2
3452690	RAPGEF3
2515783	RAPGEF4
3040967	RAPGEF5
2595560	RAPH1
3720921	RARA
2614369	RARB
3456081	RARG
3333899	RARRES3
2839671	RARS
2819044	RASA1
2645579	RASA2
3065154	RASA4
3065154	RASA4B

TCID	GENE_na29
2369110	RASAL2
3747792	RASD1
3944210	RASD2
2775259	RASGEF1B
2817941	RASGRF2
3618736	RASGRP1
2476671	RASGRP3
3867346	RASIP1
3482845	RASL11A
3286776	RASSF4
3315952	RASSF7
3464405	RASSF9
3489020	RB1
2988459	RBAK
3653317	RBBP6
4000944	RBBP7
3781429	RBBP8
3144760	RBM12B
3336402	RBM14
2675628	RBM15B
3556888	RBM23
3519119	RBM26
3976519	RBM3
3033397	RBM33
2622469	RBM5
2622469	RBM6
3959203	RBM9
3417583	RBMS2
2615060	RBMS3
2697863	RBP1
2319550	RBP7
3092415	RBPMS
3224366	RC3H2
3930235	RCAN1
2325479	RCAN3
3513794	RCBTB1
3513549	RCBTB2
2398894	RCC2
3336486	RCE1
3325503	RCN1
3602723	RCN2
2378584	RCOR3
3103293	RDH10
3416921	RDH5
3753896	RDM1
3390542	RDX
3158767	RECQL4
3248999	REEP3
2871176	REEP5
2561201	REG1P
2484358	REL
2765865	RELL1
3065740	RELN
3970214	REPS2

TCID	GENE_na29
2395245	RERE
3446297	RERGL
2728408	REST
3243846	RET
2566764	REV1
2969677	REV3L
2766359	RFC1
3433747	RFC5
2867788	RFESD
3210457	RFK
2593796	RFTN2
3625674	RFX7
3855596	RFXANK
2779335	RG9MTD2
2950590	RGL2
3639601	RGMA
2821761	RGMB
2815488	RGNEF
2499158	RGPD1
2499158	RGPD2
2499158	RGPD3
2499158	RGPD4
2499158	RGPD5
2499158	RGPD6
2372781	RGS1
3642707	RGS11
2372812	RGS13
2447148	RGS16
2372719	RGS18
3914307	RGS19
2372858	RGS2
2441386	RGS5
2463227	RGS7
2447192	RGS8
3731543	RGS9
2530330	RHBDD1
3009198	RHBDD2
3674848	RHBDF1
2674242	RHOA
2820925	RHOBTB3
2724671	RHOH
3717539	RHOT1
2384401	RHOU
4019700	RHOXF1
3978295	RIBC1
3430331	RIC8B
3397877	RICS
2510485	RIF1
4052378	RILPL1
3476212	RILPL1
3476212	RILPL2
3110395	RIMS2
3378191	RIN1
3781654	RIOK3

Figure 6 continued

TCID	GENE_na29
3555675	RNASE1
3527597	RNASE4
3527662	RNASE6
2851965	RNASEN
2984884	RNASET2
3453348	RND1
2580802	RND3
3434413	RNF10
3130850	RNF122
2647458	RNF13
3059393	RNF13
2857204	RNF138
2857204	RNF138P1
2468376	RNF144A
2897172	RNF144B
2884216	RNF145
2924898	RNF146
3927949	RNF160
3133479	RNF170
2790324	RNF175
3221571	RNF183
3146565	RNF19A
3036985	RNF216
2988459	RNF216L
3036985	RNF216L
2924253	RNF217
3895795	RNF24
3205162	RNF38
2715440	RNF4
2963929	RNGTT
3358049	RNH1
2672629	RNU13P3
3403077	RNU7
2683763	ROBO1
3354293	ROBO3
3220977	ROD1
2640263	ROPN1
2692640	ROPN1
2640263	ROPN1B
2692640	ROPN1B
2339872	ROR1
3627422	RORA
2435261	RORC
2721959	ROS1
2971378	ROS1
3098570	RP1
2960774	RP11-257K9.7
3674504	RP11-631M21.2
3514879	RP11-64P12.3
2432851	RP11-94I2.2
2357217	RP11-94I2.2
2321466	RP1-21O18.1
3975869	RP2
3896370	RP5-1022P6.2

TCID	GENE_na29
3045047	RP9
3044938	RP9
3045047	RP9P
3044938	RP9P
2346738	RPAP2
2597273	RPE
2525852	RPE
4004878	RPGR
2374956	RPL10
2331178	RPL10
2904683	RPL10A
3674146	RPL13
2618640	RPL14
3294159	RPL17
3309215	RPL17
3867223	RPL18
3309936	RPL21
3309936	RPL21P119
3309936	RPL21P134
3309936	RPL21P14
3309936	RPL21P18
3309936	RPL21P19
3309936	RPL21P28
3309936	RPL21P29
3309936	RPL21P37
3309936	RPL21P39
2769512	RPL21P44
3309936	RPL21P45
3309936	RPL21P46
3309936	RPL21P61
2898746	RPL21P68
3309936	RPL21P69
3309936	RPL21P7
3309936	RPL21P80
3309936	RPL21P93
3309936	RPL21P97
3309936	RPL21P98
3036476	RPL22
3729569	RPL23A
2390518	RPL23AP7
2390518	RPL23AP82
3174121	RPL24
3842141	RPL26
2604998	RPL3
2694706	RPL32
2694706	RPL32P3
2527196	RPL37A
3391149	RPL37AP8
2709606	RPL39L
2696309	RPL39P5
3962587	RPL5
2423175	RPL5
3797450	RPL6
3559570	RPL9

TCID	GENE_na29
2319340	RPL9P11
3257559	RPP30
3804143	RPRD1A
2358221	RPRD2
3900470	RPS15A
2686717	RPS18
2686717	RPS18P12
2686717	RPS18P5
3834465	RPS19
3961253	RPS19BP1
2331679	RPS2
3383046	RPS20P27
3892660	RPS21
2850071	RPS26
2850071	RPS26P53
2850071	RPS26P8
2330723	RPS27
2531779	RPS28
2326561	RPS6KA1
2984655	RPS6KA2
4002173	RPS6KA3
3576284	RPS6KA5
4014029	RPS6KA6
3460467	RPSAP52
2662397	RPUSD3
2964231	RRAGD
3867965	RRAS
3363868	RRAS2
3899173	RRBP1
3318009	RRM1
2469252	RRM2
3681705	RRN3
3684782	RRN3
3684548	RRN3
3962469	RRP7A
3947434	RRP7A
3947460	RRP7A
3962469	RRP7B
3947434	RRP7B
3947460	RRP7B
2675763	RRP9
2428760	RSBN1
3010030	RSBN1L
3865696	RSHL1
3037100	RSPH10B
2989316	RSPH10B
3037100	RSPH10B2
2989316	RSPH10B2
2924851	RSPO3
3662612	RSPRY1
3279575	RSU1
2348854	RTCD1
2560076	RTKN
3567050	RTN1

Figure 6 continued

TCID	GENE_na29
2967650	RTN4IP1
2657025	RTP4
2730554	RUFY3
3930360	RUNX1
3144346	RUNX1T1
2908762	RUNX2
2401994	RUNX3
3928040	RWDD2B
2749484	RXFP1
3484393	RXFP2
2805939	RXFP3
2442008	RXRG
3832457	RYR1
2387126	RYR2
4045676	S100A1
2435383	S100A10
2435410	S100A11
2435981	S100A12
4045676	S100A13
4045665	S100A14
4045643	S100A16
2436088	S100A2
4045589	S100A5
4045577	S100A6
2435989	S100A8
2359664	S100A9
2329077	S100PBP
3365249	SAAL1
2620685	SACM1L
3505319	SACS
3691326	SALL1
3150289	SAMD12
3536434	SAMD4A
3252534	SAMD8
3061456	SAMD9L
3480657	SAP18
3337618	SAPS3
3293244	SAR1A
2876257	SAR1B
2829416	SAR1B
3457201	SARNP
3470253	SART3
2930243	SASH1
3564027	SAV1
3362468	SBF2
3476130	SBNO1
3844978	SBNO2
2750594	SC4MOL
3352904	SC5DL
2817053	SCAMP1
3602004	SCAMP5
3605780	SCAND2
2621333	SCAP
2672712	SCAP

TCID	GENE_na29
3633890	SCAPER
3091475	SCARA3
3129175	SCARA5
2774049	SCARB2
3402571	SCARNA10
3442054	SCARNA11
2715076	SCARNA22
3972093	SCARNA23
2437753	SCARNA4
2703217	SCARNA7
2389789	SCCPDH
3260586	SCD
3494629	SCEL
2769182	SCFD2
2601230	SCG2
3594003	SCG3
3587495	SCG5
2898934	SCGN
2649824	SCHIP1
2990404	SCIN
2785282	SCLT1
2585400	SCN2A
2584957	SCN3A
3393622	SCN4B
2585476	SCN7A
3414969	SCN8A
2585400	SCN9A
3441885	SCNN1A
3363866	SCP2
2336585	SCP2
2794006	SCRG1
3043895	SCRN1
3760957	SCRN2
3962839	SCUBE1
3362191	SCUBE2
2904485	SCUBE3
2780734	SCYE1
3428131	SCYL2
2594812	SCYL2
2773907	SDAD1
2542795	SDC1
3108146	SDC2
2404209	SDC3
3907234	SDC4
3099750	SDCBP
3563459	SDCCAG1
3229943	SDCCAG3
3092415	SDHALP2
2987843	SDK1
2592532	SDPR
3837934	SEC1
3790479	SEC11C
3735752	SEC14L1
3942350	SEC14L2

TCID	GENE_na29
2355615	SEC22B
3561952	SEC23A
3267455	SEC23IP
2829416	SEC24A
2783316	SEC24D
3235414	SEC61A2
2651782	SEC62
3779756	SEH1L
3574207	SEL1L
2764192	SEL1L3
2443476	SELE
2435005	SELENBP1
2473784	SELI
2676901	SELK
2676927	SELK
2443450	SELL
2443417	SELP
2647792	SELT
3058759	SEMA3C
3059667	SEMA3D
3059393	SEMA3E
2361342	SEMA4A
3607927	SEMA4B
2565592	SEMA4C
4051226	SEMA4D
2692199	SEMA5B
3592755	SEMA6D
2686646	SENP7
3278234	SEPHS1
2855285	SEPP1
2764054	SEPSECS
2569908	SEPT10
2732273	SEPT11
3764527	SEPT4
3735847	SEPT9
3837504	SEPW1
2814424	SERF1A
2814424	SERF1B
3365136	SERGEF
3947434	SERHL
3947460	SERHL
3947434	SERHL2
3947460	SERHL2
2328273	SERINC2
3906942	SERINC3
2864449	SERINC5
3577612	SERPINA1
3577577	SERPINA10
3577612	SERPINA2
3549757	SERPINA3
3549740	SERPINA3
3549740	SERPINA5
2938972	SERPINB1
3791996	SERPINB8

Figure 6 continued

TCID	GENE_na29
2601414	SERPINE2
3331355	SERPING1
2651165	SERPINI1
3387259	SESN3
2589929	SESTD1
2672532	SETD2
3579205	SETD3
3930781	SETD4
2609608	SETD5
3489418	SETDB2
3228007	SETX
3687277	SEZ6L2
3667281	SF3B3
3942998	SFI1
2676518	SFMBT1
2326774	SFN
3132782	SFRP1
3966597	SFRS17A
3771800	SFRS2
2403740	SFRS4
3747324	SFRS6
3886050	SFRS6
2548970	SFRS7
2366156	SFT2D2
2948683	SFTA2
2562435	SFTPB
2842101	SFXN1
3260985	SFXN3
2768981	SGCB
2837029	SGCD
3061805	SGCE
2648535	SGEF
2340695	SGIP1
2975014	SGK1
3096545	SGK196
3101802	SGK3
3101765	SGK3
3289235	SGMS1
2738664	SGMS2
3250863	SGPL1
3568108	SGPP1
2529421	SGPP2
3431892	SH2B3
3088213	SH2D4A
3921442	SH3BGR
3226804	SH3GLB2
3717452	SH3GLP1
3304970	SH3PXD2A
2887164	SH3PXD2B
2793137	SH3RF1
2833924	SH3RF2
3380365	SHANK2
3158114	SHARPIN
3205659	SHB

TCID	GENE_na29
3708919	SHBG
2436985	SHC1
3213847	SHC3
2374926	SHISA4
2673270	SHISA5
3418007	SHMT2
2978050	SHPRH
2682568	SHQ1
3968303	SHROOM2
3354174	SIAE
2636483	SIDT1
3839619	SIGLEC12
3869097	SIGLEC6
3839619	SIGLEC7
3839619	SIGLEC9
3934111	SIK1
2877639	SIL1
3457336	SILV
3542847	SIPA1L1
2460817	SIPA1L2
3894727	SIRPA
3894727	SIRPB1
3249587	SIRT1
3357785	SIRT3
3434308	SIRT4
2895650	SIRT5
3042610	SKAP2
2651989	SKIL
2902884	SKIV2L
3154263	SLA
2440327	SLAMF1
3570266	SLC10A1
3142485	SLC10A5
2788511	SLC10A7
3454576	SLC11A2
2827525	SLC12A2
3696057	SLC12A4
3696035	SLC12A4
3617312	SLC12A6
2638728	SLC15A2
3477917	SLC15A4
2921402	SLC16A10
3981959	SLC16A2
2427469	SLC16A4
3734648	SLC16A5
3768412	SLC16A6
3290746	SLC16A9
2960955	SLC17A5
3867842	SLC17A7
3126694	SLC18A1
3935016	SLC19A1
3160658	SLC1A1
2485636	SLC1A4
2500919	SLC20A1

TCID	GENE_na29
2828479	SLC22A4
3333831	SLC22A9
2877861	SLC23A1
3622934	SLC24A5
3593014	SLC24A5
3952543	SLC25A1
2586845	SLC25A12
3062193	SLC25A13
3486728	SLC25A15
2909167	SLC25A27
2319340	SLC25A33
2645275	SLC25A36
3090006	SLC25A37
3377569	SLC25A45
3997360	SLC25A6
2756831	SLC26A1
3418394	SLC26A10
2835300	SLC26A2
3018605	SLC26A4
3106559	SLC26A7
2452754	SLC26A9
3593575	SLC27A2
2359885	SLC27A3
3872945	SLC27A5
2827645	SLC27A6
3212420	SLC28A3
2988594	SLC29A4
2409104	SLC2A1
2974935	SLC2A12
3450899	SLC2A13
4052021	SLC2A6
3622436	SLC30A4
2476116	SLC30A6
2349043	SLC30A7
2725381	SLC30A9
2701927	SLC33A1
2721959	SLC34A2
4007588	SLC35A2
2955061	SLC35B2
2940987	SLC35B3
3074039	SLC35B4
3329018	SLC35C1
3216276	SLC35D2
3389976	SLC35F2
2385967	SLC35F3
3076076	SLC37A3
3452417	SLC38A4
3769779	SLC39A11
3158581	SLC39A4
3804195	SLC39A6
3542063	SLC39A9
3333711	SLC3A2
2591837	SLC40A1
2452691	SLC41A1

Figure 6 continued

TCID	GENE_na29
3469180	SLC41A2
3373845	SLC43A3
3183111	SLC44A1
2418570	SLC44A5
3713951	SLC47A1
2512790	SLC4A10
3895330	SLC4A11
2730746	SLC4A4
2559849	SLC4A5
2831664	SLC4A9
3919033	SLC5A3
3467949	SLC5A8
3688878	SLC6A10P
3439510	SLC6A12
3439549	SLC6A13
3988165	SLC6A14
3464276	SLC6A15
3867734	SLC6A16
2799030	SLC6A19
2611848	SLC6A6
3688878	SLC6A8
2786322	SLC7A11
3087659	SLC7A2
3666146	SLC7A6
3666146	SLC7A6OS
3557209	SLC7A8
2497252	SLC9A2
3695541	SLC9A5
4006841	SLC9A7
2699145	SLC9A9
2696113	SLCO2A1
2869096	SLCO4C1
3139580	SLCO5A1
2869124	SLCO6A1
3753568	SLFN11
3753500	SLFN11
3753538	SLFN12
3753538	SLFN12L
3753568	SLFN13
3753500	SLFN13
3718555	SLFN5
3302187	SLIT1
3302056	SLIT1
2720584	SLIT2
4024685	SLITRK4
3495968	SLITRK5
3519840	SLITRK6
2625793	SLMAP
3779612	SLMO1
3911814	SLMO2
3907190	SLPI
3788302	SMAD4
3788270	SMAD4
3509842	SMAD9

TCID	GENE_na29
3454821	SMAGP
3159946	SMARCA2
3820921	SMARCA4
2745846	SMARCA5
3457455	SMARCC2
3963754	SMC1B
3182781	SMC2
3776193	SMCHD1
2553911	SMEK2
3683050	SMG1
2438042	SMG5
2371255	SMG7
2860898	SMN1
2814424	SMN1
2860898	SMN2
2814424	SMN2
2937144	SMOC2
3696317	SMPD3
2575897	SMPD4
2730404	SMR3A
2730396	SMR3A
2730404	SMR3B
2730396	SMR3B
3971387	SMS
3203382	SMU1
3014411	SMURF1
3766960	SMURF2
2464909	SMYD3
3740704	SMYD4
3876245	SNAP25
2962876	SNAP91
3163136	SNAPC3
2777714	SNCA
3022465	SND1
2607020	SNED1
3230332	SNHG7
3755198	SNIP
2407163	SNIP1
3386814	SNORA1
3230332	SNORA17
3386814	SNORA18
3309215	SNORA19
3319840	SNORA23
3386814	SNORA25
3553607	SNORA28
3453177	SNORA2A
3386814	SNORA32
3453177	SNORA34
2456849	SNORA36B
2558150	SNORA36C
3808600	SNORA37
3386814	SNORA40
2437753	SNORA42
3230332	SNORA43

TCID	GENE_na29
3693673	SNORA46
3693673	SNORA50
3359469	SNORA54
3713951	SNORA59A
3713951	SNORA59B
2841284	SNORA74B
2375706	SNORA77
3386814	SNORA8
2404254	SNORD103A
2949038	SNORD117
3851651	SNORD41
2342624	SNORD45A
2342624	SNORD45C
2444451	SNORD47
3712098	SNORD49A
3386814	SNORD5
3542847	SNORD56B
3386814	SNORD6
3371719	SNORD67
2444451	SNORD74
2444451	SNORD76
2444451	SNORD78
2444451	SNORD80
2949038	SNORD84
4017961	SNORD96B
2619666	SNRK
2565262	SNRNP200
4052378	SNRNP35
3642162	SNRPA1
3903052	SNTA1
3666601	SNTB2
3597857	SNX1
3725083	SNX11
3040073	SNX13
2963313	SNX14
3334783	SNX15
3142554	SNX16
3398482	SNX19
3597914	SNX22
3628994	SNX22
2826343	SNX24
2754582	SNX25
3830864	SNX26
2359036	SNX27
2348437	SNX7
2369557	SOAT1
3772279	SOCS3
2721633	SOD3
3301263	SORBS1
2796995	SORBS2
2797202	SORBS2
3592109	SORD
3352948	SORL1
2549092	SOS1

Figure 6 continued

TCID	GENE_na29
3960302	SOX10
2897899	SOX4
3447348	SOX5
3364306	SOX6
2603051	SP110
2531310	SP140
2531310	SP140L
2587520	SP3
2587520	SP3P
2430422	SPAG17
3742415	SPAG7
2882098	SPARC
2777113	SPARCL1
2420467	SPATA1
3481543	SPATA13
2380440	SPATA17
2726910	SPATA18
3909035	SPATA2
2742134	SPATA5
2867788	SPATA9
3413950	SPATS2
2522094	SPATS2L
2585933	SPC25
3591281	SPCS2
2752560	SPCS3
2322103	SPEN
3621948	SPG11
2834503	SPINK5
3907320	SPINLW1
3907335	SPINLW1
3590164	SPINT1
3799461	SPIRE1
2404766	SPOCD1
2876897	SPOCK1
2735027	SPP1
3623865	SPPL2A
3623472	SPPL2A
3589141	SPRED1
2556752	SPRED2
2742224	SPRY1
3519309	SPRY2
2319252	SPSB1
3190558	SPTAN1
2482505	SPTBN1
3573152	SPTLC2
3876990	SPTLC3
3114832	SQLE
3592511	SQRDL
2890239	SQSTM1
2844479	SQSTM1
2551327	SRBD1
3884191	SRC
3057668	SRCRB4D
2907730	SRF

TCID	GENE_na29
3060300	SRI
3677969	SRL
3619165	SRP14
3771297	SRP68
2382781	SRP9
2951674	SRPK1
3066297	SRPK2
3740998	SRR
3712098	SRrp35
3802129	SS18
2619323	SS18L2
3027915	SSBP1
2864849	SSBP2
2413685	SSBP3
2518428	SSFA2
3408831	SSPN
2940551	SSR1
2709750	SST
2391647	SSU72
3976559	SSX1
3976559	SSX4
4007415	SSX4
3976559	SSX4B
4007415	SSX4B
3976559	SSX5
4007415	SSX5
3976559	SSX7
4007415	SSX7
3976559	SSX8
2699145	ST13
3356175	ST14
3135046	ST18
3635198	ST20
2562529	ST3GAL5
2633256	ST3GAL6
3361971	ST5
2656837	ST6GAL1
3771712	ST6GALNAC1
3771675	ST6GALNAC2
2342904	ST6GALNAC5
3020496	ST7
3020496	ST7OT3
2868904	ST8SIA4
3429159	STAB2
2616804	STAC
2696802	STAG1
3015338	STAG3
3015338	STAG3L1
3056705	STAG3L1
3015338	STAG3L2
3056705	STAG3L2
3015338	STAG3L3
3056705	STAG3L3
3237088	STAM

TCID	GENE_na29
3257031	STAMBPL1
3094447	STAR
3508898	STARD13
2870828	STARD4
2565143	STARD7
3457752	STAT2
2592356	STAT4
3721658	STAT5A
3721658	STAT5B
3458337	STAT6
2731988	STBD1
3011838	STEAP1
3011861	STEAP2
2502762	STEAP3
2528386	STK16
2593159	STK17B
2607262	STK25
3146103	STK3
2993029	STK31
2834282	STK32A
3361811	STK33
3409081	STK38L
2402459	STMN1
3104489	STMN2
3914050	STMN3
3223928	STOM
2481379	STON1
2481379	STON1-GTF2A1L
3574121	STON2
3632806	STRA6
3766284	STRADA
2522789	STRADB
3224591	STRBP
3621351	STRC
2548274	STRN
3531163	STRN3
3852079	STX10
2327219	STX12
3891006	STX16
3819016	STXBP2
2350339	STXBP3
2929870	STXBP5
3558418	STXBP6
3513293	SUCLA2
2648098	SUCNR1
3490741	SUGT1
3486728	SUGT1L1
3102372	SULF1
3654669	SULT1A1
3656032	SULT1A1
3654669	SULT1A2
3656032	SULT1A2
3656032	SULT1A3

Figure 6 continued

TCID	GENE_na29
3656032	SULT1A4
2498911	SULT1C2
2498951	SULT1C4
3866785	SULT2A1
2955282	SUPT3H
3764384	SUPT4H1
3715703	SUPT6H
3228652	SURF1
3228621	SURF6
3220846	SUSD1
4045426	SUSD4
3236448	SUV39H2
3379390	SUV420H1
3716664	SUZ12P
2434139	SV2A
3608638	SV2B
3319997	SWAP70
2894790	SYCP2L
3466080	SYCP3
3178952	SYK
2963407	SYNCRIP
2979871	SYNE1
3539724	SYNE2
3610982	SYNM
3294668	SYNPO2L
4007899	SYP
3423622	SYT1
2361154	SYT11
3336652	SYT12
3371114	SYT13
2378256	SYT14
3287366	SYT15
3805614	SYT4
3973891	SYTL5
3377474	SYVN1
3014065	TAC1
3292946	TACR2
2414958	TACSTD2
3203199	TAF1
3361021	TAF10
3671607	TAF1C
3702382	TAF1C
3386814	TAF1D
3203199	TAF1L
2907018	TAF8
2635998	TAGLN3
2411198	TAL1
3183348	TAL2
3716048	TAOK1
2761941	TAPT1
3046520	TARP
3046708	TARP
3027961	TAS2R5
3898126	TASP1

TCID	GENE_na29
3151943	TATDN1
3422326	TBC1D15
3217184	TBC1D2
2905432	TBC1D22B
3754041	TBC1D3
3754096	TBC1D3
4040117	TBC1D3
4040849	TBC1D3
3754041	TBC1D3B
3754096	TBC1D3B
4040117	TBC1D3B
4040849	TBC1D3B
3754041	TBC1D3C
3754096	TBC1D3C
4040117	TBC1D3C
4040849	TBC1D3C
3754041	TBC1D3D
3754096	TBC1D3D
4040117	TBC1D3D
4040849	TBC1D3D
3754041	TBC1D3E
3754096	TBC1D3E
4040117	TBC1D3E
4040849	TBC1D3E
3724698	TBC1D3F
3754041	TBC1D3F
3754096	TBC1D3F
4040117	TBC1D3F
4040849	TBC1D3F
3754041	TBC1D3G
3754096	TBC1D3G
4040117	TBC1D3G
4040849	TBC1D3G
3754041	TBC1D3H
3754096	TBC1D3H
4040117	TBC1D3H
4040849	TBC1D3H
3754041	TBC1D3P2
3754096	TBC1D3P2
4040117	TBC1D3P2
4040849	TBC1D3P2
3518086	TBC1D4
2942306	TBC1D7
3986291	TBC1D8B
4002011	TBC1D8B
2709414	TBCCD1
2386418	TBCE
2738378	TBCKL
2780734	TBCKL
3419849	TBK1
3354174	TBRG1
3729834	TBX2
3982689	TBX22
3472755	TBX3

TCID	GENE_na29
3846280	TBXA2R
3027204	TBXAS1
3576704	TC2N
2989537	tcag7.903
3985644	TCEAL3
3985644	TCEAL6
3985511	TCEAL7
3969396	TCEANC
3140833	TCEB1
3590498	TCEB1
3595096	TCF12
3962338	TCF20
2926447	TCF21
3674434	TCF25
3808854	TCF4
2491386	TCF7L1
3264621	TCF7L2
3913483	TCFL5
3578152	TCL1A
3550139	TCL1B
3550139	TCL6
3374890	TCN1
3929237	TCP10L
3368520	TCP11L1
3471327	TCTN1
3429365	TDG
2909167	TDRD6
2435218	TDRKH
3320944	TEAD1
3321055	TEAD1
3401259	TEAD4
2768396	TEC
2768396	TEC
3553141	TECPR2
3165825	TEK
3415668	TENC1
3555340	TEP1
3020192	TES
3473436	TESC
3249886	TET1
2738146	TET2
3217807	TEX10
3766716	TEX2
3247784	TFAM
3247784	TFAMP1
2329920	TFAP2E
2573570	TFCP2L1
4007734	TFE3
3069082	TFEC
3933559	TFF1
3933536	TFF3
3955875	TFIP11
2591421	TFPI
3061621	TFPI2

Figure 6 continued

TCID	GENE_na29
3116614	TG
2558612	TGFA
2380590	TGFB2
3181728	TGFBR1
2615360	TGFBR2
2422722	TGFBR3
3776504	TGIF1
2562198	TGOLN2
3098935	TGS1
2550542	THADA
3067644	THAP5
3589458	THBS1
3625391	THEM4
2888103	THOC3
3956854	THOC5
3677356	THOC6
3756046	THRA
2666147	THRB
3341497	THRSP
3514879	THSD1
3514879	THSD1P
3600283	THSD4
2558511	TIA1
3309629	TIAL1
3928668	TIAM1
2932508	TIAM2
2871821	TICAM2
2333051	TIE1
2782230	TIFA
2735598	TIGD2
2883283	TIMD4
2374956	TIMM17A
3289031	TIMM23
3833093	TIMM50
3976341	TIMP1
3772661	TIMP2
3943504	TIMP3
2663130	TIMP4
3558012	TINF2
2649113	TIPARP
3693511	TIPIN
2366132	TIPRL
3355091	TIRAP
2908008	TJAP1
3615579	TJP1
3173880	TJP2
3817116	TJP3
3695107	TK2
3751042	TLCD1
3211579	TLE1
3176209	TLE4
3211579	TLE4
2750753	TLL1
3597125	TLN2

TCID	GENE_na29
2766192	TLR10
2748346	TLR2
2754937	TLR3
2766262	TLR6
3969115	TLR8
2676009	TLR9
2700365	TM4SF1
2647315	TM4SF4
3605268	TM6SF1
3448481	TM7SF3
3110608	TM7SF4
3881686	TM9SF4
3414186	TMBIM6
3635578	TMC3
3650762	TMC7
2694931	TMCC1
2376376	TMCC2
3466206	TMCC3
2442134	TMCO1
3048778	TMED4
2423264	TMED5
2871821	TMED7
3182229	TMEFF1
2592598	TMEFF2
3763390	TMEM100
3722479	TMEM106A
2990342	TMEM106B
3413278	TMEM106C
2642995	TMEM108
3471769	TMEM116
3412345	TMEM117
3388631	TMEM123
2758658	TMEM128
3478068	TMEM132D
3346147	TMEM133
3397461	TMEM135
3352485	TMEM136
3029016	TMEM139
2749380	TMEM144
3830530	TMEM147
2910364	TMEM14A
2701294	TMEM14E
2562387	TMEM150
2766289	TMEM156
2577482	TMEM163
3987029	TMEM164
3068476	TMEM168
2815220	TMEM171
2877990	TMEM173
3031624	TMEM176A
2478269	TMEM178
2537290	TMEM18
2746645	TMEM184C
3659858	TMEM188

TCID	GENE_na29
3422231	TMEM19
3039399	TMEM195
3040465	TMEM196
2925590	TMEM200A
3072435	TMEM209
3166644	TMEM215
3745525	TMEM220
2861317	TMEM30A
2725332	TMEM33
2690850	TMEM39A
2708817	TMEM41A
2611779	TMEM43
2633691	TMEM45A
4004575	TMEM47
2413423	TMEM48
3929664	TMEM50B
2409770	TMEM53
3144235	TMEM55A
2347732	TMEM56
3825244	TMEM59L
3058156	TMEM60
3591281	TMEM62
3129948	TMEM66
3136015	TMEM68
2351632	TMEM77
2427720	TMEM77
3358262	TMEM80
3316126	TMEM80
3599669	TMEM84
3620515	TMEM87A
2500615	TMEM87B
3709153	TMEM88
2450668	TMEM9
3571904	TMEM90A
3717870	TMEM98
3181240	TMOD1
3594031	TMOD2
2668205	TMPPE
2729821	TMPRSS11E
2729821	TMPRSS11E2
3393536	TMPRSS13
3351200	TMPRSS4
2491271	TMSB10
4016193	TMSB15A
4016193	TMSB15B
3449068	TMTC1
3425134	TMTC3
3812206	TMX3
3896976	TMX4
3222170	TNC
3750625	TNFAIP1
2825629	TNFAIP8
3127703	TNFRSF10B
3089816	TNFRSF10C

Figure 6 continued

TCID	GENE_na29
3150455	TNFRSF11B
3645555	TNFRSF12A
3648391	TNFRSF17
3441849	TNFRSF1A
2956052	TNFRSF21
2705706	TNFSF10
3487299	TNFSF11
3500787	TNFSF13B
3222128	TNFSF15
2444239	TNFSF18
2705266	TNIK
3085270	TNKS
3373675	TNKS1BP1
3257850	TNKS2
2342176	TNNI3K
2342220	TNNI3K
2450762	TNNT2
3317117	TNNT3
3255402	TNPO1
3851651	TNPO2
3653398	TNRC6A
3946192	TNRC6B
2599153	TNS1
3049522	TNS3
2949622	TNXA
2949622	TNXB
3762473	TOB1
3907111	TOMM34
3157385	TOP1MT
3756193	TOP2A
3748262	TOP3A
2695941	TOPBP1
2446198	TOR1AIP1
2446198	TOR1AIP2
3136888	TOX
2457842	TP53BP2
2544201	TP53I3
3145149	TP53INP1
3883013	TP53INP2
3060095	TP53TG1
2317317	TP73
2915133	TPBG
3141857	TPD52
2924330	TPD52L1
3204721	TPM2
2436526	TPM3
3823511	TPM4
2944025	TPMT
2466554	TPO
3361041	TPP1
3499453	TPP2
3843679	TPSD1
3005444	TPST1
3955915	TPST2

TCID	GENE_na29
3881443	TPX2
3528172	TRA@
3041519	TRA2A
2709062	TRA2B
3528172	TRAC
3695433	TRADD
3553337	TRAF3
2534810	TRAF3IP1
2969810	TRAF3IP2
3715839	TRAF4
2378662	TRAF5
3369890	TRAF6
3644541	TRAF7
3432267	TRAFD1
3528172	TRAJ17
2619120	TRAK1
2594812	TRAK2
3139882	TRAM1
2957227	TRAM2
3843188	TRAPPC2
3843188	TRAPPC2P1
3885223	TRAPPC6A
3155937	TRAPPC9
3528172	TRAV20
3528172	TRAV8-3
3528172	TRD@
2953570	TREM1
2953501	TREM2
2906720	TREML2
2906720	TREML2P
2906720	TREML3
2906720	TREML4
2954022	TRERF1
2954025	TRERF1
3046520	TRGC2
3046708	TRGV3
3046520	TRGV9
2641901	TRH
3115008	TRIB1
3489644	TRIM13
3217123	TRIM14
3746845	TRIM16
3746845	TRIM16L
3318443	TRIM22
3360622	TRIM22
2859734	TRIM23
2948259	TRIM26
3128954	TRIM35
2901503	TRIM39
2901503	TRIM39R
2430126	TRIM45
3360622	TRIM5
2845078	TRIM52
2390180	TRIM58

TCID	GENE_na29
3372896	TRIM77
3818515	TRIP10
2602901	TRIP12
2798915	TRIP13
3597977	TRIP4
2408111	TRIT1
3896524	TRMT6
2326846	TRNP1
2660648	TRNT1
2645951	TRPC1
3903708	TRPC4AP
4018327	TRPC5
3388438	TRPC6
3359267	TRPM5
3623771	TRPM7
3149528	TRPS1
3014411	TRRAP
3028766	TRY6
3228373	TSC1
3512294	TSC22D1
2647647	TSC22D2
3064039	TSC22D4
3365437	TSG101
2566586	TSGA10
3546213	TSHR
3794056	TSHZ1
3889419	TSHZ2
3889624	TSHZ2
3858285	TSHZ3
2503618	TSN
2334602	TSPAN1
3069955	TSPAN12
2991150	TSPAN13
2842707	TSPAN17
3458783	TSPAN31
3316375	TSPAN4
2778856	TSPAN5
4015397	TSPAN6
3974019	TSPAN7
3461981	TSPAN8
3978169	TSPYL2
3740998	TSR1
2538480	TSSC1
3620799	TTBK2
2654306	TTC14
3327948	TTC17
2585236	TTC21B
2806186	TTC23L
3721516	TTC25
3920385	TTC3
2589011	TTC30A
2588965	TTC30A
2588965	TTC30B
3111375	TTC35

Figure 6 continued

TCID	GENE_na29
2867693	TTC37
2412312	TTC39A
3199662	TTC39B
3781980	TTC39C
3333603	TTC9C
2500803	TTL
3761551	TTLL6
2420229	TTLL7
3906942	TTPAL
3783565	TTR
3734236	TTYH2
3453837	TUBA1A
3453732	TUBA1A
3453837	TUBA1B
3453732	TUBA1B
3413787	TUBA1B
3413787	TUBA1C
2575949	TUBA3C
2506185	TUBA3C
2575949	TUBA3D
2506185	TUBA3D
2575949	TUBA3E
2506185	TUBA3E
2528407	TUBA4A
2528407	TUBA4B
3936515	TUBA8
2901913	TUBB
3891342	TUBB1
2939232	TUBB2A
2939232	TUBB2B
4050485	TUBB2C
4051521	TUBB2C
2901913	TUBB2C
3674504	TUBB3
3847959	TUBB4
3674504	TUBB4Q
3779579	TUBB6
2901913	TUBBP1
2901913	TUBBP2
3764933	TUBD1
3721926	TUBG1
3721926	TUBG2
3526151	TUBGCP3
2358993	TUFT1
3401217	TULP3
3087167	TUSC3
4027769	TWF1
3451708	TWF1
2676009	TWF2
3220156	TXN
2412668	TXNDC12
2829562	TXNDC15
3707990	TXNDC17
3778589	TXNDC2

TCID	GENE_na29
2697372	TXNDC6
2644461	TXNDC6
3809324	TXNL1
3429460	TXNRD1
3775842	TYMS
3795850	TYMS
3795866	TYMS
3633794	TYRO3
3590498	TYRO3
3633794	TYRO3P
3590498	TYRO3P
3293215	TYSND1
3005995	TYW1
3055608	TYW1
3005995	TYW1B
3055608	TYW1B
3842345	U2AF2
3631397	UACA
2364189	UAP1
3976062	UBA1
3829768	UBA2
2345196	UBA2
2681195	UBA3
2695648	UBA5
2642911	UBA5
2771718	UBA6
2674762	UBA7
3498315	UBAC2
3203753	UBAP2
2360083	UBAP2L
3988674	UBE2A
2613880	UBE2E2
3072276	UBE2H
3643703	UBE2I
3771543	UBE2O
2436716	UBE2Q1
2451200	UBE2T
3097208	UBE2V2
3725481	UBE2Z
3614087	UBE3A
3431143	UBE3B
3033924	UBE3C
2319560	UBE4B
3653000	UBFD1
4027355	UBL4A
3820161	UBL5
2668351	UBP1
2437893	UBQLN4
3360553	UBQLNL
3620880	UBR1
2907190	UBR2
2399409	UBR4
3147321	UBR5
3376023	UBXN1

TCID	GENE_na29
2402601	UBXN11
2472914	UBXN2A
2507495	UBXN4
2712858	UBXN7
2725013	UCHL1
2448971	UCHL5
3381817	UCP2
3365487	UEVLD
2754673	UFSP2
2504883	UGCGL1
3521484	UGCGL2
2766456	UGDH
2485257	UGP2
2853293	UGT3A1
2853325	UGT3A2
2740507	UGT8
2364155	UHMK1
2904270	UHRF1BP1
2930957	ULBP2
2979187	ULBP2
3749010	ULK2
2670481	ULK4
3883549	UMOD
2639874	UMPS
3167731	UNC13B
2986825	UNC84A
2758602	UNC93B3
3474697	UNQ1887
2732339	UNQ3028
3629103	UNQ353
2886535	UNQ9374
3277662	UPF2
3503224	UPF3A
3351688	UPK2
3065154	UPLP
3000953	UPP1
2511712	UPP2
3652218	UQCRC2
2384705	URB2
2334279	UROD
3854311	USHBP1
3775686	USP14
3936550	USP18
3749498	USP22
3391816	USP28
3685051	USP31
3765167	USP32
3748400	USP32
2419113	USP33
2555277	USP34
2604138	USP40
3936550	USP41
3466499	USP44
2966298	USP45

Figure 6 continued

TCID	GENE_na29
3320604	USP47
2400718	USP48
3294576	USP54
3765167	USP6
3748400	USP6
3277468	USP6NL
3679564	USP7
3974708	USP9X
3974708	USP9Y
2930418	UST
3990566	UTP14A
3490504	UTP14A
3990566	UTP14C
3490504	UTP14C
3726992	UTP18
2929168	UTRN
3340697	UVRAG
3441941	VAMP1
3744217	VAMP2
2443989	VAMP4
4032755	VAMP7
2353237	VANGL1
3778601	VAPA
2902013	VARS2
3758291	VAT1
3669552	VAT1L
2426385	VAV3
3996815	VBP1
3252071	VCL
3998386	VCX
3998386	VCX2
3998386	VCX3A
3998386	VCX3B
3998386	VCY
2875954	VDAC1
3452818	VDR
2908179	VEGFA
2794792	VEGFC
2610336	VHL
2619265	VIPR1
3082373	VIPR2
2477203	VIT
3005266	VKORC1L1
3160175	VLDLR
3872274	VN1R1
2974592	VNN1
2974635	VNN2
2974610	VNN3
2675628	VPRBP
3351806	VPS11
3108901	VPS13B
3627929	VPS13C
2320762	VPS13D
3874023	VPS16A

TCID	GENE_na29
3471264	VPS29
3475545	VPS33A
3689922	VPS35
3475838	VPS37B
3620457	VPS39
7385683	VPS41
2357996	VPS45
2556215	VPS54
2434892	VPS72
3550485	VRK1
3353914	VWA5A
3441685	VWF
3240340	WAC
3298738	WAPAL
3579546	WARS
2969289	WASF1
3482572	WASF3
3445670	WBP11
3445670	WBP11P1
3771037	WBP2
3985523	WBP5
3056838	WBSCR16
3007024	WBSCR17
2601341	WDFY1
3490251	WDFY2
2776372	WDFY3
3565571	WDHD1
2760371	WDR1
2752478	WDR17
2724235	WDR19
3553017	WDR20
2725332	WDR21B
3569926	WDR22
2458082	WDR26
2354082	WDR3
2430422	WDR3
3231846	WDR37
3203855	WDR40A
2863535	WDR41
3988365	WDR44
2426840	WDR47
2704143	WDR49
3464912	WDR51B
2489228	WDR54
2673830	WDR6
3034449	WDR60
2344731	WDR63
2332999	WDR65
3730731	WDR68
3789442	WDR7
3625052	WDR72
2417016	WDR78
2676041	WDR82
3607766	WDR93

TCID	GENE_na29
3593770	WDSOF1
3886938	WFDC2
3907320	WFDC6
3907348	WFDC8
2715076	WHSC1
3460198	WIF1
2587841	WIPF1
2995076	WIPF3
3768474	WIPI1
3400034	WNK1
4009604	WNK3
2528159	WNT10A
2677356	WNT5A
2830598	WNT8A
3715109	WSB1
3430620	WSCD2
2753732	WWC2
3968397	WWC3
3669650	WWOX
3105777	WWP1
3977862	XAGE1A
3977862	XAGE1B
3977862	XAGE1C
3977862	XAGE1D
3977862	XAGE1E
3956589	XBP1
3989678	XIAP
2513758	XIRP2
4015548	XKRX
3216969	XPA
2663810	XPC
3946510	XPNPEP3
3961699	XPNPEP3
2555490	XPO1
3686339	XPO6
3088983	XPO7
2370123	XPR1
2818454	XRCC4
2526980	XRCC6
3879467	XRN2
3451264	YAF2
2929870	YAP1
2405192	YARS
2329077	YARS
3639601	YBX2
2923060	YDD19
2655168	YEATS2
3832280	YIF1B
2413484	YIPF1
2879509	YIPF5
3825838	YJEFN3
3240012	YME1L1
3938244	YPEL1
4024373	YTHDC2

Figure 6 continued

TCID	GENE_na29
2824483	YTHDC2
2327630	YTHDF2
3886639	YWHAB
3943207	YWHAH
2539869	YWHAQ
2437577	YY1AP1
2437645	YY1AP1
3971329	YY2
3813604	ZADH2
2704052	ZBBX
2688499	ZBED2
3349719	ZBTB16
3989089	ZBTB33
3458216	ZBTB39
3189580	ZBTB43
3398241	ZBTB44
2571217	ZC3H8
2412834	ZCCHC11
3988596	ZCCHC12
3703665	ZCCHC14
3987607	ZCCHC16
3791341	ZCCHC2
3296981	ZCCHC24
2721809	ZCCHC4
2818079	ZCCHC9
3063968	ZCWPW1
3322958	ZDHHC13
2933175	ZDHHC14
3504691	ZDHHC20
3199431	ZDHHC21
3331433	ZDHHC5
3307120	ZDHHC6
4021341	ZDHHC9
3241316	ZEB1
2579572	ZEB2
2528308	ZFAND2B
2905664	ZFAND3
3462094	ZFC3H1
3797015	ZFP161
3842794	ZFP28
3860954	ZFP30
3569754	ZFP36L1
3331730	ZFP91
3331730	ZFP91-CNTF
3110789	ZFPM2
3971923	ZFX
3971923	ZFY
2817731	ZFYVE16
3619650	ZFYVE19
3590129	ZFYVE19
3553947	ZFYVE21
3260018	ZFYVE27
2757796	ZFYVE28
3906062	ZHX3

TCID	GENE_na29
3872053	ZIM2
3015147	ZKSCAN1
2706791	ZMAT3
3132616	ZMAT4
3460129	ZMYM2
4011889	ZMYM3
2329752	ZMYM4
2408929	ZMYND12
3908149	ZMYND8
3053380	ZNF117
3849549	ZNF121
2465551	ZNF124
2808290	ZNF131
3872928	ZNF132
3843742	ZNF135
3855985	ZNF14
3319898	ZNF143
3835318	ZNF155
3976240	ZNF157
2900195	ZNF165
3819968	ZNF177
3829857	ZNF181
2900423	ZNF187
2900372	ZNF193
3359751	ZNF195
2620160	ZNF197
3717635	ZNF207
3856646	ZNF208
3856720	ZNF208
3910260	ZNF217
3244539	ZNF22
3835318	ZNF221
3835418	ZNF224
3835494	ZNF226
3835565	ZNF233
3835467	ZNF234
3285614	ZNF25
3826041	ZNF253
3872560	ZNF256
3826803	ZNF257
3392871	ZNF259
3657367	ZNF267
3004768	ZNF273
3019401	ZNF277
4021508	ZNF280C
3625823	ZNF280D
3933399	ZNF295
3063646	ZNF3
2881607	ZNF300
3829857	ZNF302
3869714	ZNF320
2946500	ZNF322A
2946500	ZNF322B
2947248	ZNF323

TCID	GENE_na29
2745220	ZNF330
3159013	ZNF34
2842860	ZNF346
3870135	ZNF347
3818842	ZNF358
2862019	ZNF366
3831475	ZNF382
3129361	ZNF395
3803882	ZNF397
3803882	ZNF397OS
3793888	ZNF407
3872335	ZNF416
3843275	ZNF419
3826656	ZNF429
3856720	ZNF43
3826306	ZNF43
3677592	ZNF434
3283613	ZNF438
3851454	ZNF443
3991992	ZNF449
3078774	ZNF467
3842839	ZNF470
3244055	ZNF487
3826803	ZNF492
3216476	ZNF510
2474651	ZNF512
3840795	ZNF525
3843386	ZNF530
3866649	ZNF541
3843848	ZNF544
3843188	ZNF547
3843214	ZNF548
3872441	ZNF552
3819968	ZNF559
3849797	ZNF561
3849797	ZNF562
3849549	ZNF562
3860824	ZNF569
3114820	ZNF572
3864430	ZNF575
3842315	ZNF580
3842301	ZNF581
3871903	ZNF582
2390976	ZNF596
3213530	ZNF598
3869714	ZNF600
3872604	ZNF606
3869714	ZNF611
3747324	ZNF624
3826041	ZNF626
3826079	ZNF626
2331903	ZNF643
2422517	ZNF644
3761737	ZNF652

Figure 6 continued

TCID	GENE_na29
3014904	ZNF655
3206317	ZNF658
3206317	ZNF658B
3826306	ZNF66
2619521	ZNF662
3871935	ZNF667
2465493	ZNF670
3857171	ZNF675
3856720	ZNF676
2402691	ZNF683
3687910	ZNF689
2465493	ZNF695
3849549	ZNF699
3657367	ZNF720
3657318	ZNF720
2756309	ZNF721
3856720	ZNF728
3078656	ZNF746
3843275	ZNF749
4023006	ZNF75D
3840795	ZNF761
3840795	ZNF765
3078656	ZNF767
3872274	ZNF772
3860999	ZNF781
3030585	ZNF783
3014808	ZNF789
3851464	ZNF799
3843906	ZNF8
2518889	ZNF804A
3011675	ZNF804B
3872441	ZNF814
3718382	ZNF830
3871903	ZNF835
3688381	ZNF843
3840795	ZNF845
3849549	ZNF846
3826306	ZNF85
3826079	ZNF90
3005069	ZNF92
3826079	ZNF93
3826803	ZNF98
3856720	ZNF99
3826803	ZNF99
2420958	ZNHIT6
3668834	ZNRF1
2995076	ZNRF2
3057755	ZP3
3057668	ZP3
2462693	ZP4
3050170	ZPBP
2577700	ZRANB3
2900269	ZSCAN16
3391769	ZW10

TCID	GENE_na29
3290210	ZWINT
2336539	ZYG11A
3741875	ZZEF1

Figure 6 continued

CEL File	Subtype Pathology	Simplified Pathology
151276HUEX1A11.CEL	FA	B
151279HUEX1A11.CEL	FA	B
151326HUEX1A11.CEL	FA	B
151329HUEX1A11.CEL	FA	B
151345HUEX1A11.CEL	FA	B
151356HUEX1A11.CEL	FA	B
151359HUEX1A11.CEL	FA	B
151361HUEX1A11.CEL	FA	B
151364HUEX1A11.CEL	FA	B
151793HUEX1A11.CEL	FA	B
151794HUEX1A11.CEL	FA	B
151795HUEX1A11.CEL	FA	B
151797HUEX1A11.CEL	FA	B
151798HUEX1A11.CEL	FA	B
151799HUEX1A11.CEL	FA	B
151800HUEX1A11.CEL	FA	B
151801HUEX1A11.CEL	FA	B
151802HUEX1A11.CEL	FA	B
151803HUEX1A11.CEL	FA	B
151804HUEX1A11.CEL	FA	B
151805HUEX1A11.CEL	FA	B
151806HUEX1A11.CEL	FA	B
151285HUEX1A11.CEL	LCT	B
151291HUEX1A11.CEL	LCT	B
151294HUEX1A11.CEL	LCT	B
151295HUEX1A11.CEL	LCT	B
151305HUEX1A11.CEL	LCT	B
151309HUEX1A11.CEL	LCT	B
151316HUEX1A11.CEL	LCT	B
151336HUEX1A11.CEL	LCT	B
151338HUEX1A11.CEL	LCT	B
151373HUEX1A11.CEL	LCT	B
151860HUEX1A11.CEL	LCT	B

Figure 7

151862HUEX1A11.CEL	LCT	B
151863HUEX1A11.CEL	LCT	B
151864HUEX1A11.CEL	LCT	B
151865HUEX1A11.CEL	LCT	B
151868HUEX1A11.CEL	LCT	B
151871HUEX1A11.CEL	LCT	B
151872HUEX1A11.CEL	LCT	B
151876HUEX1A11.CEL	LCT	B
151881HUEX1A21.CEL	LCT	B
151883HUEX1A11.CEL	LCT	B
151890HUEX1A11.CEL	LCT	B
151895HUEX1A11.CEL	LCT	B
151896HUEX1A11.CEL	LCT	B
151897HUEX1A11.CEL	LCT	B
151899HUEX1A11.CEL	LCT	B
151902HUEX1A11.CEL	LCT	B
151908HUEX1A11.CEL	LCT	B
151909HUEX1A11.CEL	LCT	B
151911HUEX1A11.CEL	LCT	B
151912HUEX1A11.CEL	LCT	B
151913HUEX1A11.CEL	LCT	B
151914HUEX1A11.CEL	LCT	B
151915HUEX1A11.CEL	LCT	B
151916HUEX1A11.CEL	LCT	B
151918HUEX1A11.CEL	LCT	B
151919HUEX1A11.CEL	LCT	B
151920HUEX1A11.CEL	LCT	B
151923HUEX1A11.CEL	LCT	B
151275HUEX1A11.CEL	NHP	B
151283HUEX1A11.CEL	NHP	B
151284HUEX1A11.CEL	NHP	B
151289HUEX1A11.CEL	NHP	B
151293HUEX1A11.CEL	NHP	B
151306HUEX1A11.CEL	NHP	B

Figure 7 Continued

151308HUEX1A11.CEL	NHP	B
151315HUEX1A11.CEL	NHP	B
151325HUEX1A11.CEL	NHP	B
151330HUEX1A11.CEL	NHP	B
151380HUEX1A11.CEL	NHP	B
151751HUEX1A11.CEL	NHP	B
151752HUEX1A11.CEL	NHP	B
151753HUEX1A11.CEL	NHP	B
151754HUEX1A11.CEL	NHP	B
151757HUEX1A11.CEL	NHP	B
151759HUEX1A11.CEL	NHP	B
151760HUEX1A11.CEL	NHP	B
151762HUEX1A11.CEL	NHP	B
151763HUEX1A11.CEL	NHP	B
151779HUEX1A11.CEL	NHP	B
151787HUEX1A11.CEL	NHP	B
151788HUEX1A11.CEL	NHP	B
151875HUEX1A11.CEL	NHP	B
151340HUEX1A11.CEL	ATC	M
151354HUEX1A11.CEL	ATC	M
151879HUEX1A11.CEL	ATC	M
151886HUEX1A11.CEL	ATC	M
151887HUEX1A11.CEL	ATC	M
151278HUEX1A11.CEL	FC	M
151281HUEX1A11.CEL	FC	M
151317HUEX1A11.CEL	FC	M
151323HUEX1A11.CEL	FC	M
151334HUEX1A11.CEL	FC	M
151362HUEX1A11.CEL	FC	M
151365HUEX1A11.CEL	FC	M
151840HUEX1A21.CEL	FC	M
151842HUEX1A11.CEL	FC	M
151843HUEX1A11.CEL	FC	M
151844HUEX1A11.CEL	FC	M

Figure 7 Continued

151846HUEX1A11.CEL	FC	M
151847HUEX1A11.CEL	FC	M
151848HUEX1A11.CEL	FC	M
151849HUEX1A11.CEL	FC	M
151851HUEX1A11.CEL	FC	M
151852HUEX1A11.CEL	FC	M
151857HUEX1A11.CEL	FC	M
151859HUEX1A11.CEL	FC	M
151321HUEX1A11.CEL	FVPTC	M
151339HUEX1A11.CEL	FVPTC	M
151341HUEX1A11.CEL	FVPTC	M
151347HUEX1A11.CEL	FVPTC	M
151348HUEX1A11.CEL	FVPTC	M
151358HUEX1A11.CEL	FVPTC	M
151363HUEX1A11.CEL	FVPTC	M
151367HUEX1A11.CEL	FVPTC	M
151368HUEX1A11.CEL	FVPTC	M
151819HUEX1A11.CEL	FVPTC	M
151820HUEX1A11.CEL	FVPTC	M
151824HUEX1A11.CEL	FVPTC	M
151825HUEX1A11.CEL	FVPTC	M
151828HUEX1A11.CEL	FVPTC	M
151829HUEX1A11.CEL	FVPTC	M
151831HUEX1A11.CEL	FVPTC	M
151832HUEX1A11.CEL	FVPTC	M
151834HUEX1A11.CEL	FVPTC	M
151836HUEX1A11.CEL	FVPTC	M
151850HUEX1A11.CEL	FVPTC	M
151856HUEX1A11.CEL	FVPTC	M
151277HUEX1A11.CEL	HC	M
151318HUEX1A11.CEL	HC	M
151352HUEX1A11.CEL	HC	M
151375HUEX1A11.CEL	HC	M
151780HUEX1A11.CEL	HC	M

Figure 7 Continued

151781HUEX1A11.CEL	HC	M
151782HUEX1A11.CEL	HC	M
151783HUEX1A11.CEL	HC	M
151784HUEX1A11.CEL	HC	M
151785HUEX1A11.CEL	HC	M
151786HUEX1A11.CEL	HC	M
151789HUEX1A11.CEL	HC	M
151791HUEX1A11.CEL	HC	M
151792HUEX1A11.CEL	HC	M
151808HUEX1A11.CEL	HC	M
151809HUEX1A11.CEL	HC	M
151810HUEX1A11.CEL	HC	M
151811HUEX1A11.CEL	HC	M
151812HUEX1A11.CEL	HC	M
151813HUEX1A11.CEL	HC	M
151814HUEX1A11.CEL	HC	M
151861HUEX1A21.CEL	HC	M
151877HUEX1A11.CEL	HC	M
151901HUEX1A11.CEL	HC	M
151906HUEX1A11.CEL	HC	M
151917HUEX1A11.CEL	HC	M
151921HUEX1A11.CEL	HC	M
151300HUEX1A11.CEL	MTC	M
151304HUEX1A11.CEL	MTC	M
151376HUEX1A11.CEL	MTC	M
151773HUEX1A11.CEL	MTC	M
151774HUEX1A11.CEL	MTC	M
151775HUEX1A11.CEL	MTC	M
151776HUEX1A11.CEL	MTC	M
151777HUEX1A11.CEL	MTC	M
151869HUEX1A11.CEL	MTC	M
151874HUEX1A11.CEL	MTC	M
151878HUEX1A11.CEL	MTC	M
151880HUEX1A12.CEL	MTC	M

Figure 7 Continued

151882HUEX1A11.CEL	MTC	M
151884HUEX1A11.CEL	MTC	M
151888HUEX1A11.CEL	MTC	M
151889HUEX1A11.CEL	MTC	M
151891HUEX1A11.CEL	MTC	M
151892HUEX1A11.CEL	MTC	M
151893HUEX1A11.CEL	MTC	M
151898HUEX1A11.CEL	MTC	M
151903HUEX1A11.CEL	MTC	M
151905HUEX1A11.CEL	MTC	M
151286HUEX1A11.CEL	PTC	M
151288HUEX1A11.CEL	PTC	M
151297HUEX1A11.CEL	PTC	M
151319HUEX1A11.CEL	PTC	M
151320HUEX1A11.CEL	PTC	M
151324HUEX1A11.CEL	PTC	M
151344HUEX1A11.CEL	PTC	M
151346HUEX1A11.CEL	PTC	M
151350HUEX1A11.CEL	PTC	M
151353HUEX1A11.CEL	PTC	M
151379HUEX1A11.CEL	PTC	M
151382HUEX1A12.CEL	PTC	M
151384HUEX1A11.CEL	PTC	M
151816HUEX1A11.CEL	PTC	M
151817HUEX1A11.CEL	PTC	M
151818HUEX1A11.CEL	PTC	M
151821HUEX1A11.CEL	PTC	M
151826HUEX1A11.CEL	PTC	M
151827HUEX1A11.CEL	PTC	M
151833HUEX1A11.CEL	PTC	M
151835HUEX1A11.CEL	PTC	M
151838HUEX1A11.CEL	PTC	M
151839HUEX1A11.CEL	PTC	M
151841HUEX1A11.CEL	PTC	M

Figure 7 Continued

151866HUEX1A21.CEL	PTC	M
151894HUEX1A11.CEL	PTC	M

Figure 7 Continued

CEL File Name	Subtype Pathology	Simplified Pathology
F0012001	B	B
F0012002	B	B
F0012003	B	B
F0012004	B	B
F0012005	FA	B
F0012006	FA	B
F0012007	FA	B
F0012008	FA	B
F0012009	FA	B
F0012010	FA	B
F0012011	FA	B
F0012012	FA	B
F0012013	FA	B
F0012014	FA	B
F0012015	FA	B
F0012016	FA	B
F0012017	FC	M
F0012018	FC	M
F0012019	FC	M
F0012020	FC	M
F0012021	FVPTC	M
F0012022	FVPTC	M
F0012023	FVPTC	M
F0012024	HA	B
F0012025	HA	B
F0012026	HA	B
F0012027	HC	M
F0012028	MTC	M
F0012029	NHP	B
F0012030	NHP	B
F0012031	NHP	B
F0012032	NHP	B
F0012033	NHP	B

Figure 8

F0012034	NHP	B
F0012035	NHP	B
F0012036	NHP	B
F0012037	NHP	B
F0012038	NHP	B
F0012039	NHP	B
F0012040	NHP	B
F0012041	NHP	B
F0012042	NHP	B
F0012043	NHP	B
F0012044	NHP	B
F0012045	NHP	B
F0012046	NHP	B
F0012047	NHP	B
F0012048	NHP	B
F0012049	NHP	B
F0012050	NHP	B
F0012051	NHP	B
F0012052	NHP	B
F0012053	NHP	B
F0012054	PTC	M
F0012055	PTC	M
F0012056	PTC	M
F0012057	PTC	M
F0012058	PTC	M
F0012059	PTC	M
F0012060	PTC	M
F0012061	PTC	M
F0012062	PTC	M
F0012063	PTC	M
F0012064	PTC	M
F0012065	PTC	M
F0012066	PTC	M
F0012067	PTC	M

Figure 8 Continued

F0012068	PTC	M
F0012069	PTC	M
F0012070	PTC	M
F0012071	PTC	M
F0012072	PTC	M
F0012073	PTC	M
F0012074	PTC	M

Figure 8 Continued

Rank	Gene Symbol	TCID	Ref Seq
1	SEMA3D	3059667	NM_152754
2	MT1G	3692999	NM_005950
3	MGC26647	3060450	BC028365
4	CLDN16	2657808	NM_006580
5	DPP4	2584018	NM_001935
6	LIPH	2708855	NM_139248
7	TM7SF4	3110608	NM_030788
8	RAG2	3369931	NM_000536
9	SLC26A4	3018605	NM_000441
10	STK32A	2834282	NM_001112724
11	CD36	3010503	NM_001001548
12	PLA2R1	2583374	NM_007366
13	ELMO1	3046197	NM_014800
14	TCID2526806	2526806	unknown
15	NELL2	3451814	NM_006159
16	CXCL9	2773947	NM_002416
17	CYSLTR2	3489138	NM_020377
18	LONRF2	2567167	NM_198461
19	TMSL8	4016193	NM_021992
20	CXCL13	2732508	NM_006419
21	RGS13	2372812	NM_002927
22	PSD3	3126191	NM_015310
23	TNFRSF17	3648391	NM_001192
24	TSPAN8	3461981	NM_004616
25	CXCL11	2773972	NM_005409
26	AIM2	2439554	NM_004833
27	ERO1LB	2462329	NM_019891
28	TRPC5	4018327	NM_012471
29	TC2N	3576704	NM_152332
30	PIP3-E	2980449	NM_015553
31	ZMAT4	3132616	NM_024645
32	PTPRC	2373842	NM_002838
33	RHOBTB3	2820925	NM_014899

Figure 9

34	TIMP1	3976341	NM_003254
35	MPZL2	3393720	NM_144765
36	IL7R	2806468	NM_002185
37	SLC4A4	2730746	NM_001098484
38	MYEF2	3622934	NM_016132
39	LGALS2	3960174	NM_006498
40	KCNA3	2427619	NM_002232
41	PDE5A	2783596	NM_001083
42	COP1	3389450	NM_052889
43	ANK2	2740067	NM_001148
44	EPS8	3445908	NM_004447
45	PLAG1	3136178	NM_002655
46	TLR10	2766192	NM_030956
47	IGF2BP2	2708922	NM_006548
48	PDK4	3062082	NM_002612
49	TMEM100	3763390	NM_001099640
50	SLC5A8	3467949	NM_145913
51	KLRG1	3404030	NM_005810
52	CP	2700244	NM_000096
53	RYR2	2387126	NM_001035
54	TMEM171	2815220	NM_173490
55	BHLHB2	2608725	NM_003670
56	ARNTL	3321150	NM_001178
57	GBP5	2422035	NM_052942
58	CYSLTR1	4013460	NM_006639
59	ACBD7	3279058	NM_001039844
60	LYPLA1	3135567	NM_006330
61	GABBR2	3217242	NM_005458
62	ITGA4	2518272	NM_000885
63	PLEKHF2	3107828	NM_024613
64	LOC401498	3166644	NM_212558
65	CASP1	3389353	NM_033292
66	MLLT3	3200982	NM_004529
67	CMAH	2945882	NR_002174

Figure 9 Continued

68	ITPR1	2608469	NM_001099952
69	GLDC	3197955	NM_000170
70	LRRN3	3019158	NM_001099660
71	TMEM156	2766289	NM_024943
72	ATP8A1	2767378	NM_006095
73	CSGALNACT1	3126504	NM_018371
74	PYHIN1	2362351	NM_152501
75	ZNF208	3856646	ENST00000340708
76	DOCK8	3159330	NM_203447
77	JAK2	3160895	NM_004972
78	SORBS2	2796995	NM_021069
79	CD2	2353669	NM_001767
80	RHOH	2724671	NM_004310
81	PLEK	2486811	NM_002664
82	ABCD2	3450861	NM_005164
83	PRICKLE1	3451375	NM_153026
84	KLRB1	3443804	NM_002258
85	STK17B	2593159	NM_004226
86	CD69	3443868	NM_001781
87	PGCP	3108226	NM_016134
88	NOD1	3044072	NM_006092
89	ENTPD1	3259253	NM_001776
90	C1orf34	2412312	NM_001080494
91	CCDC146	3009838	NM_020879
92	LRRN1	2608309	NM_020873
93	C12orf35	3410384	NM_018169
94	ANXA1	3174816	NM_000700
95	CAMK4	2823880	NM_001744
96	EFEMP1	2554018	NM_004105
97	SPP1	2735027	NM_001040058
98	C17orf87	3742627	AY358809
99	SEPP1	2855285	NM_001093726
100	PTPN22	2428796	NM_015967

Figure 9 Continued

Rank	Gene Symbol	TCID	P value	Fold Change
1	SCG3	3594003	5.77E-85	6.20
2	SYT4	3805614	9.65E-75	4.17
3	SCG2	2601230	3.63E-74	4.42
4	DNAJC12	3292413	5.07E-74	3.19
5	CHGB	3875179	5.06E-73	5.88
6	NEFM	3090436	7.29E-71	4.39
7	INA	3262129	2.30E-70	3.95
8	KIAA1409	3549264	3.73E-70	2.55
9	CALCA	3364127	1.40E-68	5.73
10	CEACAM5	3834341	3.01E-67	5.55
11	ASCL1	3429008	4.03E-66	3.61
12	SNAP25	3876245	1.66E-65	3.59
13	RAB3C	2810805	3.32E-65	3.53
14	SCN9A	2585400	7.04E-62	3.02
15	RGS7	2463227	2.08E-61	1.66
16	ST18	3135046	1.42E-60	2.82
17	SCGN	2898934	2.82E-60	3.54
18	PCSK1	2868044	1.02E-59	2.76
19	NRXN1	2552643	2.31E-59	2.61
20	PRUNE2	3210497	1.82E-58	3.59
21	C19orf30	3817651	3.45E-58	2.35
22	C6orf117	2915571	5.01E-58	2.60
23	SLC2A12	2974935	6.94E-57	2.57
24	FMN2	2387711	1.73E-56	3.36
25	OR10G9	3353876	9.70E-56	3.20
26	NOL4	3803628	1.75E-54	2.87
27	JAKMIP2	2880361	2.69E-54	2.35
28	DNAJC6	2340350	3.61E-54	1.98
29	SYT1	3423622	4.31E-54	3.36
30	CYP3A5	3063406	4.63E-54	1.78
31	HMP19	2841802	1.19E-53	2.68
32	GRP	3790529	1.80E-53	2.40

Figure 10

33	RET	3243846	3.10E-53	1.51
34	KIAA1244	2927604	9.26E-53	1.44
35	CNTN1	3411721	4.37E-52	3.20
36	GRIA3	3989448	1.14E-51	3.33
37	TSHZ2	3889419	2.00E-51	2.79
38	PRUNE2	3210616	2.04E-51	3.06
39	FSTL5	2791894	6.58E-51	3.82
40	EDN3	3891447	9.93E-51	2.76
41	LGR5	3422144	1.11E-50	2.72
42	PBOV1	2976417	1.80E-50	2.78
43	GALNT13	2511045	2.24E-50	3.28
44	CADPS	2679406	1.85E-49	1.77
45	PHYHIPL	3247977	1.88E-49	2.51
46	GRM8	3071063	5.28E-49	2.00
47	CNKSR3	2980516	2.30E-48	1.22
48	MEIS2	3618333	1.00E-47	1.99
49	HPGD	2794408	2.06E-47	3.40
50	DCX	4018218	3.69E-47	1.72
51	CA8	3137120	4.13E-47	1.55
52	FGF9	3480885	5.66E-47	2.32
53	DNER	2602770	5.94E-47	1.12
54	NCALD	3147173	9.64E-47	2.43
55	TMEM16D	3428333	1.65E-46	2.58
56	AMPH	3046739	4.08E-46	1.19
57	SLC4A10	2512790	5.70E-46	3.37
58	BAALC	3110217	1.01E-45	1.31
59	TCID2525682	2525682	3.54E-45	1.06
60	KCND2	3021009	2.13E-44	2.12
61	ADCYAP1	3775906	2.25E-44	1.61
62	CACNA2D2	2675315	3.53E-43	1.43
63	REST	2728408	4.17E-43	-1.61
64	PCDHB10	2832423	8.03E-43	1.94
65	TMEM196	3040465	8.87E-43	2.51
66	BMP5	2958172	1.37E-42	3.04

Figure 10 Continued

67	SEMA3E	3059393	1.70E-42	3.94
68	PPFIA2	3463821	1.83E-42	2.46
69	GRIA2	2749222	7.09E-42	2.32
70	CACNG2	3959787	8.76E-42	1.90
71	PRKAR2B	3018375	1.91E-41	2.78
72	KCNB2	3103062	6.57E-41	1.26
73	PACRG	2935311	8.69E-41	1.64
74	HMGCLL1	2958117	1.08E-40	1.83
75	WASF1	2969289	2.12E-40	1.78
76	CNTNAP2	3029900	5.87E-40	1.54
77	DDC	3050388	5.92E-40	1.24
78	FGF14	3523499	8.04E-40	1.77
79	NEFL	3128271	9.05E-40	1.89
80	MAP1B	2814756	6.91E-39	2.48
81	CPLX2	2842255	9.32E-39	1.03
82	FMO5	2433232	1.57E-38	2.36
83	CHGA	3549092	2.07E-38	1.05
84	CEACAM6	3834379	2.57E-38	3.14
85	CHST9	3802416	2.96E-38	2.39
86	PON3	3061964	5.03E-38	2.97
87	TSHR	3546213	5.91E-38	-4.16
88	DNAH5	2849056	1.67E-37	1.66
89	GAP43	2637112	1.91E-37	2.66
90	GCH1	3565524	5.81E-37	2.77
91	KCNH8	2613293	9.06E-37	1.04
92	TFF1	3933559	2.55E-36	2.60
93	PCDHB4	2832315	2.72E-36	1.74
94	KCNJ15	3920850	3.35E-36	-2.85
95	PON1	3061942	4.75E-36	1.61
96	RIMS2	3110395	8.47E-36	3.17
97	TXNDC13	3896976	1.11E-35	1.77
98	GPX2	3568603	1.16E-35	2.28
99	NKAIN2	2924081	1.40E-35	2.01
100	TMOD1	3181240	1.40E-35	2.35

Figure 10 Continued

Rank	Gene Symbol	TCID	Ref Seq
1	NRCAM	3067478	NM_001037132
2	DOCK9	3522398	NM_015296
3	CAMK2N1	2400177	NM_018584
4	C6orf168	2966193	NM_032511
5	SCEL	3494629	NM_144777
6	SIPA1L2	2460817	NM_020808
7	IL1RAP	2657831	NM_002182
8	PPM2C	3107342	NM_018444
9	RHOBTB3	2820925	NM_014899
10	AMOT	4018454	NM_133265
11	SDC4	3907234	NM_002999
12	MET	3020343	NM_001127500
13	DCBLD2	2686023	NM_080927
14	SYTL5	3973891	NM_138780
15	AHNAK2	3581221	NM_138420
16	MYH10	3744463	NM_005964
17	TCID2526806	2526806	unknown
18	TACSTD2	2414958	NM_002353
19	PROS1	2685304	NM_000313
20	ERBB3	3417249	NM_001982
21	EPS8	3445908	NM_004447
22	XPR1	2370123	NM_004736
23	KRT19	3757108	NM_002276
24	7A5	3040518	NM_182762
25	FN1	2598261	NM_212482
26	GABBR2	3217242	NM_005458
27	TRAK2	2594812	NM_015049
28	GABRB2	2884845	NM_021911
29	GALNT7	2751936	NM_017423
30	IGFBP6	3415744	NM_002178
31	NELL2	3451814	NM_006159
32	SGEF	2648535	NM_015595
33	SLC47A1	3713951	NM_018242

Figure 11

34	PDZRN4	3411810	NM_013377
35	MPZL2	3393720	NM_144765
36	CMYA5	2817464	NM_153610
37	ARMCX6	4015838	NM_019007
38	SLC34A2	2721959	NM_006424
39	MPPED2	3367673	NM_001584
40	TUSC3	3087167	NM_006765
41	DTNA	3784208	NM_032975
42	FAM176A	2560625	NM_032181
43	C5orf28	2855578	BC013351
44	CYSLTR2	3489138	NM_020377
45	S100A5	4045589	NM_002962
46	PDE5A	2783596	NM_001083
47	KCNJ2	3733275	NM_000891
48	AK1	3226138	NM_000476
49	LIPH	2708855	NM_139248
50	MPP7	3282601	NM_173496
51	CSNK1G3	2826550	NM_004384
52	ZCCHC16	3987607	NM_001004308
53	PSD3	3126191	NM_015310
54	BHLHB2	2608725	NM_003670
55	EGFR	3002640	NM_005228
56	SERPINA1	3577612	NM_001002236
57	ITGA3	3726154	NM_002204
58	CSGALNACT1	3126504	NM_018371
59	CHI3L1	2451593	NM_001276
60	METTL7B	3416895	NM_152637
61	TGFA	2558612	NM_003236
62	NAB2	3417809	NM_005967
63	NFATC3	3666033	NM_173163
64	NPC2	3571904	NM_006432
65	GGCT	3044129	ENST00000275428
66	TPO	2466554	NM_000547
67	HGD	4047070	NM_000187

Figure 11 Continued

68	GIMAP5	3031573	NM_018384
69	PKHD1L1	3111561	NM_177531
70	ALDH3A2	3714068	NM_001031806
71	PRR15	2994981	NM_175887
72	HRASLS3	3376529	NM_007069
73	ZCCHC12	3988596	NM_173798
74	STK32A	2834282	NM_001112724
75	ANK2	2740067	NM_001148
76	SORBS2	2796995	NM_021069
77	ITGA2	2809245	NM_002203
78	MYEF2	3622934	NM_016132
79	SYNE1	2979871	NM_182961
80	PLEKHA4	3867458	NM_020904
81	PLCD3	3759587	NM_133373
82	LAMB3	2453793	NM_001017402
83	FAM43A	2658785	NM_153690
84	TPD52L1	2924330	NM_001003395
85	CLDN1	2710599	NM_021101
86	B3GNT3	3824596	NM_014256
87	KIAA1217	3238962	NM_019590
88	MAP2	2525533	NM_002374
89	LRP1B	2578790	NM_018557
90	ITPR1	2608469	NM_001099952
91	CARD8	3866958	NM_014959
92	DGKI	3074912	NM_004717
93	LIFR	2854092	NM_002310
94	DOCK8	3159330	NM_203447
95	C9orf61	3173974	NM_004816
96	GPR98	2819779	NM_032119
97	TFF3	3933536	NM_003226
98	ERO1LB	2462329	NM_019891
99	ARHGAP24	2734421	NM_001025616
100	CDON	3396770	NM_016952
101	TBC1D4	3518086	NM_014832

Figure 11 Continued

102	LRP2	2586038	NM_004525

Figure 11 Continued

Rank	Gene Symbol	TCID
1	TGFA	2558612
2	PROS1	2685304
3	MET	3020343
4	DPP4	2584018
5	GALNT7	2751936
6	TPO	2466554
7	SDC4	3907234
8	FABP4	3142381
9	KIT	2727587
10	ELMO1	3046197
11	CDH3	3666366
12	CAMK2N1	2400177
13	KRT19	3757108
14	SCEL	3494629
15	TFF3	3933536
16	LRP1B	2578790
17	CITED1	4012178
18	PLA2R1	2583374
19	STK32A	2834282
20	IL1RAP	2657831
21	LGALS3	3536706
22	GPR155	2587790
23	MPPED2	3367673
24	C6orf168	2966193
25	METTL7B	3416895
26	NPC2	3571904
27	NAB2	3417809
28	KHDRBS2	2959039
29	LIPH	2708855
30	CXorf27	3973891
31	FN1	2598261
32	EPS8	3445908
33	ZMAT4	3132616

Figure 12

34	SLC26A4	3018605
35	TNFRSF11B	3150455
36	ANGPTL1	2445982
37	NFATC3	3666033
38	ITPR1	2608469
39	GABRB2	2884845
40	TBC1D4	3518086
41	SCG5	3587495
42	CYP1B1	2548699
43	HMGA2	3420316
44	TC2N	3576704
45	ATP10D	2726072
46	RAG2	3369931
47	DUSP6	3464860
48	ERO1LB	2462329
49	SCNN1A	3441885
50	ABCC3	3726691
51	ARHGAP24	2734421
52	SEMA3D	3059667
53	CHI3L1	2451593
54	SPOCK1	2876897
55	PDE5A	2783596
56	MYH10	3744463
57	SERPINA1	3577612
58	SIPA1L2	2460817
59	ITM2A	4013549
60	TNFAIP8	2825629
61	MYEF2	3622934
62	KCNJ2	3733275
63	CRABP1	3603295
64	MATN2	3108526
65	CLDN16	2657808
66	NRCAM	3067478
67	HEY2	2924492

Figure 12 Continued

68	PTTG1	2838201
69	SPINT1	3590164
70	CDC27	3760625
71	NOD1	3044072
72	KPNA5	2922840
73	DYNLT1	2981874
74	ODZ1	4020655
75	GABBR2	3217242
76	SLC33A1	2701927
77	UPP1	3000953
78	AUTS2	3006572
79	SLC34A2	2721959
80	MFGE8	3638204
81	RXRG	2442008
82	KLF8	3978943
83	ANK2	2740067
84	TM7SF4	3110608
85	ZCCHC16	3987607
86	FNDC4	2545953
87	GLT8D2	3468888
88	GDF15	3824993
89	GIMAP8	3031466
90	MAP2	2525533
91	TIMP1	3976341
92	PGCP	3108226
93	KLK7	3868783
94	DNASE1L3	2678298
95	ANKRD12	3778252
96	CLDN1	2710599
97	SERINC2	2328273
98	HSD17B6	3417703
99	TSC22D1	3512294
100	TRPC5	4018327

Figure 12 Continued

TCID	Gene_Symbol	Subtype 1	Subtype 2	Subtype 3
3132616	ZMAT4	FA_FVPTC	FA_PTC	FVPTC_NHP
2809793	GZMK	FC_LCT	FVPTC_LCT	HC_LCT
3444086	KLRK1	FC_LCT	FVPTC_LCT	HC_LCT
2959039	KHDRBS2	FA_FC	FA_HC	HC_NHP
2657808	CLDN16	FA_FC	FA_PTC	LCT_PTC
4020655	ODZ1	FA_FC	FVPTC_LCT	LCT_PTC
3692999	MT1G	FA_MTC	FA_PTC	MTC_NHP
2710599	CLDN1	FA_FC	FA_PTC	NHP_PTC
3536706	LGALS3	FA_FVPTC	FA_PTC	NHP_PTC
3577612	SERPINA1	FA_FVPTC	FA_PTC	NHP_PTC
2727587	KIT	FA_FVPTC	FVPTC_NHP	NHP_PTC
3367673	MPPED2	FA_PTC	FVPTC_NHP	NHP_PTC
2884845	GABRB2	FA_PTC	LCT_PTC	NHP_PTC
2685304	PROS1	FA_PTC	LCT_PTC	NHP_PTC
3564210	PYGL	ATC_FA	ATC_LCT	
3168508	MELK	ATC_FA	ATC_NHP	
3913483	TCFL5	FA_FC	FA_FVPTC	
3726691	ABCC3	FA_FC	FA_PTC	
3662201	MT1H	FA_FC	FA_PTC	
3369931	RAG2	FA_FC	FA_PTC	
2573570	TFCP2L1	FA_FC	FA_PTC	
2466554	TPO	FA_FC	FA_PTC	
3944404	APOL1	FA_FVPTC	FA_PTC	
3451814	NELL2	FA_FVPTC	FA_PTC	
3592214	DUOX1	FA_HC	FVPTC_LCT	
2809810	GZMA	FC_LCT	FVPTC_LCT	
3018605	SLC26A4	FA_FC	FVPTC_NHP	
3755862	IKZF3	FA_PTC	HC_LCT	
2373842	PTPRC	FC_LCT	HC_LCT	
3443891	CLEC2B	FVPTC_LCT	HC_LCT	
3031556	GIMAP2	FVPTC_LCT	HC_LCT	
3031517	GIMAP7	FVPTC_LCT	HC_LCT	
3160895	JAK2	FVPTC_LCT	HC_LCT	

Figure 13

3666033	NFATC3	FVPTC_LCT	HC_LCT
3417703	HSD17B6	FA_HC	HC_NHP
3875179	CHGB	FA_MTC	LCT_MTC
2834282	STK32A	FA_FC	LCT_PTC
2751936	GALNT7	FA_PTC	LCT_PTC
2708855	LIPH	FA_PTC	LCT_PTC
3393720	MPZL2	FA_PTC	LCT_PTC
3464860	DUSP6	FVPTC_LCT	LCT_PTC
3416895	METTL7B	FVPTC_LCT	LCT_PTC
2711225	ATP13A4	FVPTC_LCT	MTC_NHP
3364127	CALCA	LCT_MTC	MTC_NHP
2526806	2526806	FA_PTC	NHP_PTC
3430462	BTBD11	FA_PTC	NHP_PTC
3086809	C8orf79	FA_PTC	NHP_PTC
3396770	CDON	FA_PTC	NHP_PTC
2584018	DPP4	FA_PTC	NHP_PTC
2598261	FN1	FA_PTC	NHP_PTC
2378068	G0S2	FA_PTC	NHP_PTC
3925639	NRIP1	FA_PTC	NHP_PTC
3270270	PTPRE	FA_PTC	NHP_PTC
2721959	SLC34A2	FA_PTC	NHP_PTC
2730746	SLC4A4	FA_PTC	NHP_PTC
2796995	SORBS2	FA_PTC	NHP_PTC
3976341	TIMP1	FA_PTC	NHP_PTC
2455933	ESRRG	FVPTC_NHP	NHP_PTC
2819779	GPR98	FVPTC_NHP	NHP_PTC
2578790	LRP1B	FVPTC_NHP	NHP_PTC
2586038	LRP2	FVPTC_NHP	NHP_PTC
3108526	MATN2	FVPTC_NHP	NHP_PTC
4014029	RPS6KA6	FVPTC_NHP	NHP_PTC
2961177	COL12A1	ATC_LCT	
3590014	CASC5	ATC_NHP	
3258444	CEP55	ATC_NHP	
3565663	DLG7	ATC_NHP	

Figure 13 Continued

2838656	HMMR	ATC_NHP
3258168	KIF11	ATC_NHP
3312490	MKI67	ATC_NHP
3776139	NDC80	ATC_NHP
3590388	NUSAP1	ATC_NHP
3881443	TPX2	ATC_NHP
2406391	2406391	FA_FC
2445982	ANGPTL1	FA_FC
3459722	AVPR1A	FA_FC
3124344	C8orf15	FA_FC
3107234	C8orf39	FA_FC
3010503	CD36	FA_FC
3580769	CKB	FA_FC
3603295	CRABP1	FA_FC
2336891	DIO1	FA_FC
3384704	DLG2	FA_FC
2678298	DNASE1L3	FA_FC
2981874	DYNLT1	FA_FC
3008144	EIF4H	FA_FC
2462329	ERO1LB	FA_FC
4027639	F8	FA_FC
3142381	FABP4	FA_FC
3576749	FBLN5	FA_FC
3937967	FLJ26056	FA_FC
3393479	FXYD6	FA_FC
3197140	GLIS3	FA_FC
3250278	HK1	FA_FC
2770469	IGFBP7	FA_FC
2452440	KLHDC8A	FA_FC
3067302	LAMB1	FA_FC
2854092	LIFR	FA_FC
3745525	LOC388335	FA_FC
3244055	LOC439911	FA_FC
3788097	MAPK4	FA_FC

Figure 13 Continued

2581000	NEB	FA_FC
2980449	PIP3-E	FA_FC
2955827	PLA2G7	FA_FC
3009229	POR	FA_FC
2349848	PRMT6	FA_FC
3555675	RNASE1	FA_FC
2984884	RNASET2	FA_FC
3363868	RRAS2	FA_FC
3899173	RRBP1	FA_FC
2387126	RYR2	FA_FC
3365136	SERGEF	FA_FC
2529421	SGPP2	FA_FC
3921442	SH3BGR	FA_FC
2319340	SLC25A33	FA_FC
3114832	SQLE	FA_FC
2932508	TIAM2	FA_FC
3943504	TIMP3	FA_FC
3388438	TRPC6	FA_FC
2538480	TSSC1	FA_FC
3441941	VAMP1	FA_FC
2331558	BMP8A	FA_HC
2648991	KCNAB1	FA_HC
2931172	IYD	FA_MTC
3661718	LPCAT2	FA_MTC
3889419	TSHZ2	FA_MTC
3040518	7A5	FA_PTC
2991233	AHR	FA_PTC
3244622	ALOX5	FA_PTC
3627248	ANXA2	FA_PTC
3848039	C3	FA_PTC
2739160	CCDC109B	FA_PTC
2902844	CFB	FA_PTC
2451593	CHI3L1	FA_PTC
3129065	CLU	FA_PTC

Figure 13 Continued

3335894	CST6	FA_PTC
3385769	CTSC	FA_PTC
3634811	CTSH	FA_PTC
2773434	CXCL2	FA_PTC
3973891	CXorf27	FA_PTC
2548699	CYP1B1	FA_PTC
3489138	CYSLTR2	FA_PTC
3768535	FAM20A	FA_PTC
3306984	GPAM	FA_PTC
3727583	HLF	FA_PTC
3820443	ICAM1	FA_PTC
3415744	IGFBP6	FA_PTC
2657831	IL1RAP	FA_PTC
3787187	KATNAL2	FA_PTC
2764192	KIAA0746	FA_PTC
3978943	KLF8	FA_PTC
3757108	KRT19	FA_PTC
2634091	NFKBIZ	FA_PTC
2639054	PARP14	FA_PTC
3111561	PKHD1L1	FA_PTC
3977067	PLP2	FA_PTC
3426502	PLXNC1	FA_PTC
3930360	RUNX1	FA_PTC
2908762	RUNX2	FA_PTC
3106559	SLC26A7	FA_PTC
2827645	SLC27A6	FA_PTC
3907190	SLPI	FA_PTC
2491271	TMSB10	FA_PTC
2353669	CD2	FC_LCT
2440354	CD48	FC_LCT
2326463	CD52	FC_LCT
2773947	CXCL9	FC_LCT
2854327	FYB	FC_LCT
2903401	HLA-DPB1	FC_LCT

Figure 13 Continued

3315675	IFITM1	FC_LCT
2772566	IGJ	FC_LCT
2563785	IGK@	FC_LCT
3512874	LCP1	FC_LCT
3421511	LYZ	FC_LCT
2519480	GULP1	FC_NHP
3110789	ZFPM2	FC_NHP
3288518	C10orf72	FVPTC_LCT
3410384	C12orf35	FVPTC_LCT
3338192	CCND1	FVPTC_LCT
3622239	DUOXA1	FVPTC_LCT
3217242	GABBR2	FVPTC_LCT
2587790	GPR155	FVPTC_LCT
3482888	GTF3A	FVPTC_LCT
3323052	NAV2	FVPTC_LCT
2562529	ST3GAL5	FVPTC_LCT
2825629	TNFAIP8	FVPTC_LCT
2705706	TNFSF10	FVPTC_LCT
2448971	UCHL5	FVPTC_LCT
2740067	ANK2	FVPTC_NHP
3802396	AQP4	FVPTC_NHP
2515183	C2orf37	FVPTC_NHP
2855578	C5orf28	FVPTC_NHP
2742581	FAT4	FVPTC_NHP
2726542	FLJ21511	FVPTC_NHP
2583374	PLA2R1	FVPTC_NHP
2699623	PLSCR4	FVPTC_NHP
3513549	RCBTB2	FVPTC_NHP
2336539	ZYG11A	FVPTC_NHP
2439554	AIM2	HC_LCT
3945651	APOBEC3G	HC_LCT
3302187	ARHGAP19	HC_LCT
3267314	BAG3	HC_LCT
3635198	BCL2A1	HC_LCT

Figure 13 Continued

3866958	CARD8	HC_LCT
3389353	CASP1	HC_LCT
3393744	CD3D	HC_LCT
2635741	CD96	HC_LCT
3187577	CEP110	HC_LCT
3815399	CNN2	HC_LCT
3629811	DENND4A	HC_LCT
3159330	DOCK8	HC_LCT
2424524	DPYD	HC_LCT
2739308	EGF	HC_LCT
2997907	EPDR1	HC_LCT
3397589	ETS1	HC_LCT
2422035	GBP5	HC_LCT
3031573	GIMAP5	HC_LCT
3982612	GPR174	HC_LCT
2362394	IFI16	HC_LCT
3918447	IFNAR2	HC_LCT
2806468	IL7R	HC_LCT
4013549	ITM2A	HC_LCT
3404030	KLRG1	HC_LCT
2508520	KYNU	HC_LCT
2531310	LOC93349	HC_LCT
4037595	ND1	HC_LCT
3256590	PAPSS2	HC_LCT
3772525	PSCD1	HC_LCT
2362351	PYHIN1	HC_LCT
2592356	STAT4	HC_LCT
3576704	TC2N	HC_LCT
3176209	TLE4	HC_LCT
2579572	ZEB2	HC_LCT
3319898	ZNF143	HC_LCT
3197231	C9orf68	HC_NHP
2750627	CPE	HC_NHP
3108226	PGCP	HC_NHP

Figure 13 Continued

3301713	BLNK	LCT_MTC
3110395	RIMS2	LCT_MTC
3594003	SCG3	LCT_MTC
2966193	C6orf168	LCT_PTC
3445908	EPS8	LCT_PTC
2708922	IGF2BP2	LCT_PTC
3126191	PSD3	LCT_PTC
3183757	RAD23B	LCT_PTC
2711205	ATP13A4	MTC_NHP
3486096	FREM2	MTC_NHP
2734421	ARHGAP24	NHP_PTC
2763278	GPR125	NHP_PTC
3625271	RAB27A	NHP_PTC
3059667	SEMA3D	NHP_PTC

Figure 13 Continued

Sample ID	Sample Type	Subtype Pathology	Simplified Pathology
A0017251	FNA	FA	B
A0017252	FNA	FA	B
A0017255	FNA	FA	B
A0017256	FNA	FA	B
A0017264	FNA	FA	B
A0017267	FNA	FA	B
A0017272	FNA	FA	B
A0017285	FNA	FA	B
A0017289	FNA	FA	B
A0017291	FNA	FA	B
A0017292	FNA	FA	B
A0017298	FNA	FA	B
A0017978	FNA	FA	B
A0017986	FNA	FA	B
A0017987	FNA	FA	B
A0017989	FNA	FA	B
A0017991	FNA	FA	B
A0017995	FNA	FA	B
A0018000	FNA	FA	B
A0018004	FNA	FA	B
A0018006	FNA	FA	B
A0018008	FNA	FA	B
A0018010	FNA	FA	B
A0018011	FNA	FA	B
A0018018	FNA	FA	B
A0017258	FNA	NHP	B
A0017265	FNA	NHP	B
A0017271	FNA	NHP	B
A0017275	FNA	NHP	B
A0017276	FNA	NHP	B
A0017278	FNA	NHP	B
A0017280	FNA	NHP	B

Figure 14

A0017295	FNA	NHP	B
A0017296	FNA	NHP	B
A0017297	FNA	NHP	B
A0017299	FNA	NHP	B
A0017979	FNA	NHP	B
A0017980	FNA	NHP	B
A0017983	FNA	NHP	B
A0017984	FNA	NHP	B
A0017985	FNA	NHP	B
A0017988	FNA	NHP	B
A0017993	FNA	NHP	B
A0017994	FNA	NHP	B
A0017997	FNA	NHP	B
A0017998	FNA	NHP	B
A0018009	FNA	NHP	B
A0018020	FNA	NHP	B
A0018021	FNA	NHP	B
A0018022	FNA	NHP	B
A0017270	FNA	FC	M
A0017294	FNA	FC	M
A0017981	FNA	FC	M
A0018016	FNA	FC	M
A0018023	FNA	FC	M
A0018025	FNA	FC	M
A0017269	FNA	FVPTC	M
A0017279	FNA	FVPTC	M
A0017982	FNA	FVPTC	M
A0017999	FNA	FVPTC	M
A0017268	FNA	MTC	M
A0017250	FNA	PTC	M
A0017253	FNA	PTC	M
A0017254	FNA	PTC	M
A0017257	FNA	PTC	M
A0017266	FNA	PTC	M

Figure 14 Continued

A0017273	FNA	PTC	M
A0017274	FNA	PTC	M
A0017281	FNA	PTC	M
A0017282	FNA	PTC	M
A0017284	FNA	PTC	M
A0017286	FNA	PTC	M
A0017290	FNA	PTC	M
A0017293	FNA	PTC	M
A0017990	FNA	PTC	M
A0017992	FNA	PTC	M
A0017996	FNA	PTC	M
A0018001	FNA	PTC	M
A0018002	FNA	PTC	M
A0018003	FNA	PTC	M
A0018005	FNA	PTC	M
A0018007	FNA	PTC	M
A0018012	FNA	PTC	M
A0018014	FNA	PTC	M
A0018015	FNA	PTC	M
A0018017	FNA	PTC	M
A0018019	FNA	PTC	M
A0018024	FNA	PTC	M
A0018027	FNA	PTC	M

Figure 14 Continued

Sample ID	Sample Type	Subtype	Simplified Pathology
miR101	FNA	PTC	M
miR102	FNA	NHP	B
miR103	FNA	PTC	M
miR104	FNA	BN	B
miR105	FNA	BN	B
miR106	FNA	LCT	B
miR107	FNA	LCT	B
miR108	FNA	BN	B
miR109	FNA	PTC	M
miR110	FNA	FVPTC	M
miR111	FNA	LCT	B
miR112	FNA	PTC	M
miR113	FNA	BN	B
miR114	FNA	NHP	B
miR115	FNA	CN	B
miR116	FNA	B	B
miR117	FNA	NHP	B
miR118	FNA	CN	B
miR119	FNA	PTC	M
miR120	FNA	PTC	M
miR121	FNA	non-diagnostic	non-diagnostic
miR122	FNA	NHP	B
miR123	FNA	NHP	B
miR124	FNA	NHP	B

Figure 15

miRNA	CHR	*P*	DE
hsa-miR-127-5p	14	0.0011	-1
hsa-miR-154	14	0.0032	-1
hsa-miR-29b-1*	7	0.0311	-1
hsa-miR-220a	X	0.0347	-1
hsa-miR-370	14	0.0779	-1
hsa-miR-96*	7	0.0843	-1
hsa-miR-197	1	0.1004	1
hsa-miR-220c	19	0.1137	-1
hsa-miR-19a	13	0.1159	1
hsa-miR-339-3p	7	0.1218	1
hsa-miR-146a*	5	0.1388	1
hsa-miR-200b*	1	0.1577	1
hsa-miR-200b	1	0.1584	1

Figure 16

miRNA	PROBE ID	CHR	*P*	DE	Rep
hsa-miR-542-5p	ILMN_3167175	X	0.0020	0.378	1
hsa-miR-191*	ILMN_3167124	3	0.0023	-0.192	ND
hsa-miR-577	ILMN_3167406	4	0.0023	-0.229	1
hsa-miR-542-3p	ILMN_3167074	X	0.0040	0.284	0.55
hsa-miR-604	ILMN_3167804	10	0.0041	-0.376	0.95
hsa-miR-125a-5p	ILMN_3167670	19	0.0041	0.099	0.95
hsa-miR-27b	ILMN_3168409	9	0.0045	0.134	1
hsa-miR-551b	ILMN_3166993	3	0.0051	0.776	1
hsa-miR-563	ILMN_3167408	3	0.0052	-0.087	ND
hsa-miR-424	ILMN_3166938	X	0.0054	0.138	0.59
hsa-miR-135b	ILMN_3167874	1	0.0057	0.261	1
hsa-miR-197	ILMN_3167864	1	0.0058	-0.090	ND
hsa-miR-221*	ILMN_3168580	X	0.0064	0.410	1
hsa-miR-221	ILMN_3167681	X	0.0065	0.062	1
HS_107	ILMN_3167213	0	0.0066	-0.173	1
hsa-miR-429	ILMN_3167806	1	0.0068	0.344	0.77
hsa-miR-99a	ILMN_3168213	21	0.0069	0.176	0.86
hsa-miR-31	ILMN_3167837	9	0.0069	0.313	1
HS_131	ILMN_3168028	0	0.0071	-0.207	0.91
hsa-miR-200b	ILMN_3168294	1	0.0075	0.227	0.5
hsa-miR-302c	ILMN_3166944	4	0.0081	-0.307	1
hsa-miR-181a-2*	ILMN_3168577	9	0.0082	0.186	1
hsa-miR-130b*	ILMN_3168588	22	0.0085	-0.178	1
hsa-let-7e	ILMN_3168463	19	0.0089	0.084	0.5
hsa-miR-218	ILMN_3168380	4,5	0.0097	0.209	0.91
hsa-miR-133b	ILMN_3168348	6	0.0100	0.279	0.95
hsa-miR-125b	ILMN_3168389	21,11	0.0102	0.080	ND
hsa-miR-1296	ILMN_3167351	10	0.0105	0.384	ND
hsa-miR-222	ILMN_3167963	X	0.0109	0.138	1
hsa-miR-222*	ILMN_3168712	X	0.0110	0.192	1
hsa-miR-450a	ILMN_3168187	X,X	0.0111	0.186	ND
hsa-miR-31*	ILMN_3168847	9	0.0113	0.388	1
hsa-let-7i*	ILMN_3168724	12	0.0113	0.225	0.77

Figure 17

HS_73.1	ILMN_3167416	0	0.0119	0.482	1
hsa-miR-200a	ILMN_3167801	1	0.0121	0.416	ND
hsa-miR-922	ILMN_3168748	3	0.0123	-0.074	ND
hsa-miR-136*	ILMN_3168667	14	0.0131	0.224	ND
hsa-miR-1231	ILMN_3167675	1	0.0132	0.113	ND
hsa-miR-224	ILMN_3168515	X	0.0144	0.326	0.95
hsa-miR-146b-5p	ILMN_3167894	10	0.0148	0.290	1
hsa-miR-141*	ILMN_3168669	12	0.0148	0.368	ND
hsa-miR-708	ILMN_3168563	11	0.0150	0.348	ND
hsa-miR-296-3p	ILMN_3168049	20	0.0186	0.253	0.64
hsa-miR-125b-2*	ILMN_3168804	21	0.0187	0.319	ND
hsa-miR-608	ILMN_3167500	10	0.0191	-0.464	1
HS_162	ILMN_3167742	0	0.0194	0.313	1
hsa-miR-200c*	ILMN_3168701	12	0.0201	0.232	0.82
hsa-miR-141	ILMN_3168064	12	0.0205	0.183	ND
HS_151.1	ILMN_3167470	0	0.0207	-0.483	1
hsa-miR-451	ILMN_3167614	17	0.0209	-0.027	ND
hsa-miR-424*	ILMN_3168638	X	0.0219	0.286	ND
hsa-miR-26b	ILMN_3167374	2	0.0223	-0.021	ND
hsa-miR-150*	ILMN_3168730	19	0.0224	-0.265	ND
hsa-miR-361-3p	ILMN_3168815	X	0.0228	-0.188	0.95
HS_120	ILMN_3166997	0	0.0229	-0.183	ND
hsa-miR-495	ILMN_3167052	14	0.0241	0.096	ND
hsa-miR-519e*	ILMN_3168031	19	0.0256	-0.269	0.73
HS_101	ILMN_3167526	0	0.0256	-0.175	ND
hsa-miR-1226	ILMN_3168807	3	0.0266	-0.267	ND
hsa-miR-576-3p	ILMN_3168559	4	0.0272	-0.188	0.77
hsa-miR-146a*	ILMN_3168687	5	0.0272	-0.276	ND
hsa-miR-28-3p	ILMN_3168657	3	0.0273	-0.121	ND
hsa-miR-1178	ILMN_3168877	12	0.0285	0.316	ND
hsa-miR-146b-3p	ILMN_3168841	10	0.0289	0.225	1
HS_130	ILMN_3168254	0	0.0294	-0.183	ND
hsa-miR-203	ILMN_3167375	14	0.0320	0.229	ND
hsa-miR-1250	ILMN_3168585	17	0.0329	-0.168	ND

Figure 17 Continued

hsa-miR-16	ILMN_3167989	3,13	0.0334	-0.032	ND
HS_196.1	ILMN_3166967	0	0.0344	0.209	0.82
HS_266.1	ILMN_3168251	0	0.0364	0.320	ND
hsa-let-7a*	ILMN_3168708	22,9	0.0370	0.232	ND
HS_48.1	ILMN_3167790	0	0.0371	0.249	1
solexa-7111-119	ILMN_3168909	0	0.0378	0.151	ND
hsa-miR-766	ILMN_3167038	X	0.0386	-0.248	ND
hsa-miR-450b-5p	ILMN_3168884	X	0.0386	0.111	ND
solexa-555-1991	ILMN_3168904	0	0.0387	-0.080	ND
hsa-miR-663	ILMN_3167088	20	0.0400	-0.468	0.91
hsa-miR-99b	ILMN_3168262	19	0.0405	0.209	ND
hsa-miR-382	ILMN_3167239	14	0.0409	0.114	ND
hsa-miR-27b*	ILMN_3168599	9	0.0422	0.140	0.86
hsa-miR-566	ILMN_3167704	3	0.0424	-0.194	ND
hsa-miR-452	ILMN_3167050	X	0.0426	0.175	ND
hsa-miR-125a-3p	ILMN_3168574	19	0.0458	0.180	ND
hsa-miR-206	ILMN_3168019	6	0.0467	0.251	ND
hsa-miR-509-3p	ILMN_3168363	X,X,X	0.0470	0.183	ND
hsa-miR-342-5p	ILMN_3168614	14	0.0477	-0.154	ND
hsa-miR-23b	ILMN_3167997	9	0.0500	0.035	ND
hsa-miR-24-1*	ILMN_3168844	9	0.0504	0.289	ND
hsa-miR-200c	ILMN_3167002	12	0.0524	0.092	ND
hsa-miR-1293	ILMN_3168857	12	0.0524	0.169	ND
HS_231	ILMN_3167534	0	0.0525	0.251	ND
hsa-miR-372	ILMN_3167184	19	0.0533	-0.087	ND
hsa-miR-335	ILMN_3167996	7	0.0535	0.077	ND
hsa-miR-193a-3p	ILMN_3168366	17	0.0548	0.113	0.86
hsa-miR-200a*	ILMN_3167179	1	0.0551	0.227	ND
hsa-miR-1297	ILMN_3168867	13	0.0551	0.089	ND
HS_284.1	ILMN_3168214	0	0.0558	-0.156	ND
HS_86	ILMN_3167504	0	0.0558	0.106	0.64
hsa-miR-1180	ILMN_3168881	17	0.0567	-0.097	ND
hsa-miR-187	ILMN_3168167	18	0.0575	0.164	ND
hsa-miR-135a	ILMN_3167823	3,12	0.0601	0.146	ND

Figure 17 Continued

hsa-miR-943	ILMN_3168720	4	0.0605	-0.076	ND
hsa-miR-1279	ILMN_3168811	12	0.0615	-0.211	ND
hsa-miR-657	ILMN_3167034	17	0.0615	-0.063	ND
hsa-miR-15a*	ILMN_3168662	13	0.0617	0.218	ND
hsa-miR-449b	ILMN_3168441	5	0.0634	-0.076	ND
HS_208	ILMN_3167907	0	0.0635	0.064	ND
hsa-miR-489	ILMN_3167272	7	0.0641	0.335	ND
hsa-miR-155*	ILMN_3168715	21	0.0671	-0.207	ND
hsa-miR-511	ILMN_3167598	10,10	0.0680	0.208	ND
HS_116	ILMN_3167951	0	0.0682	-0.235	ND
hsa-miR-34a	ILMN_3168429	1	0.0695	0.189	ND
HS_38.1	ILMN_3168353	0	0.0717	-0.114	ND
hsa-miR-708*	ILMN_3168647	11	0.0719	0.110	ND
HS_35	ILMN_3167886	0	0.0732	0.153	ND
hsa-miR-515-5p	ILMN_3166959	19,19	0.0748	-0.254	ND
HS_3	ILMN_3168047	0	0.0755	1.395	ND
HS_166.1	ILMN_3168315	0	0.0793	-0.134	ND
HS_156	ILMN_3168305	0	0.0794	0.250	ND
hsa-miR-376a*:9.1	ILMN_3167419	0	0.0798	0.218	ND
solexa-5169-164	ILMN_3168902	0	0.0822	0.167	ND
HS_8	ILMN_3167836	0	0.0825	0.188	ND
hsa-miR-556-5p	ILMN_3167655	1	0.0836	0.175	ND
hsa-miR-375	ILMN_3167229	2	0.0845	0.174	ND
hsa-miR-520f	ILMN_3167075	19	0.0858	0.208	ND
hsa-miR-1321	ILMN_3168663	X	0.0859	-0.122	ND
hsa-miR-548f	ILMN_3168534	5,X,2,7,10	0.0869	0.087	ND
hsa-let-7i	ILMN_3168316	12	0.0879	0.017	ND
hsa-miR-151-3p	ILMN_3168705	8	0.0888	0.065	ND
hsa-miR-561	ILMN_3167109	2	0.0890	-0.157	ND
HS_12	ILMN_3168104	0	0.0904	0.192	ND
hsa-miR-212	ILMN_3167761	17	0.0907	0.213	ND
hsa-miR-505	ILMN_3168412	X	0.0913	-0.203	ND
hsa-miR-524-5p	ILMN_3168284	19	0.0918	0.207	ND
hsa-miR-744*	ILMN_3168733	17	0.0930	0.173	ND

Figure 17 Continued

hsa-miR-148b*	ILMN_3168567	12	0.0937	0.112	ND
hsa-miR-155	ILMN_3168170	21	0.0942	-0.119	ND
HS_89	ILMN_3168065	0	0.0944	0.138	ND
HS_267	ILMN_3167573	0	0.0948	-0.094	ND
hsa-miR-630	ILMN_3167844	15	0.0959	-0.282	ND
hsa-miR-33a	ILMN_3167691	22	0.0969	0.237	ND
HS_106	ILMN_3167464	0	0.0976	-0.119	ND
HS_57.1	ILMN_3167398	0	0.0992	-0.212	ND
hsa-miR-658	ILMN_3168097	22	0.0999	0.244	ND
hsa-miR-101*	ILMN_3168196	1	0.1001	0.119	ND

Figure 17 Continued

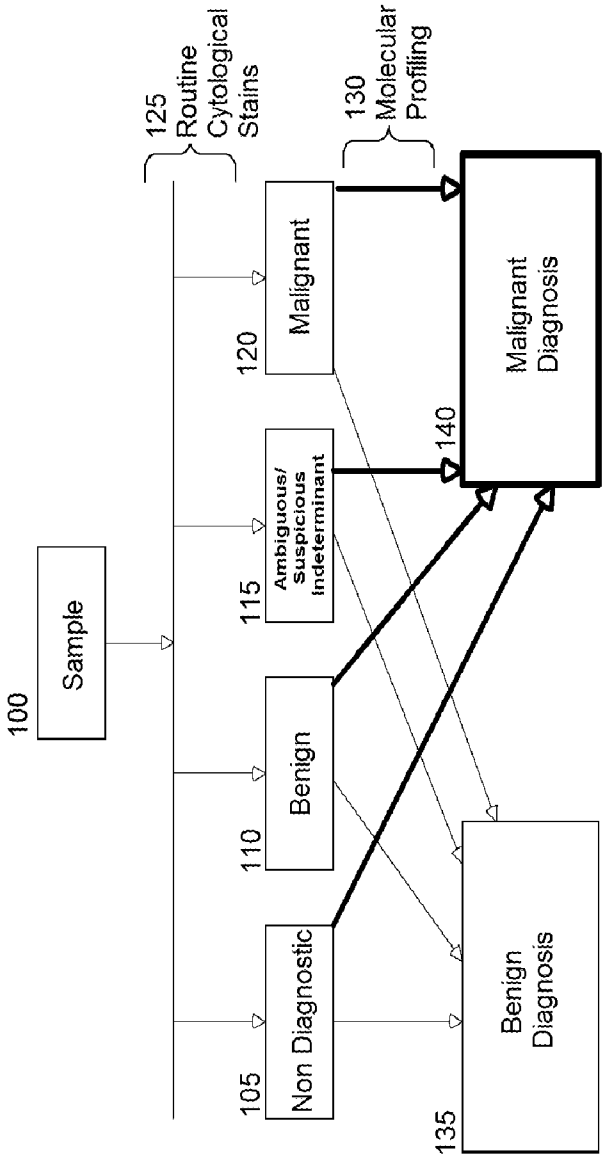
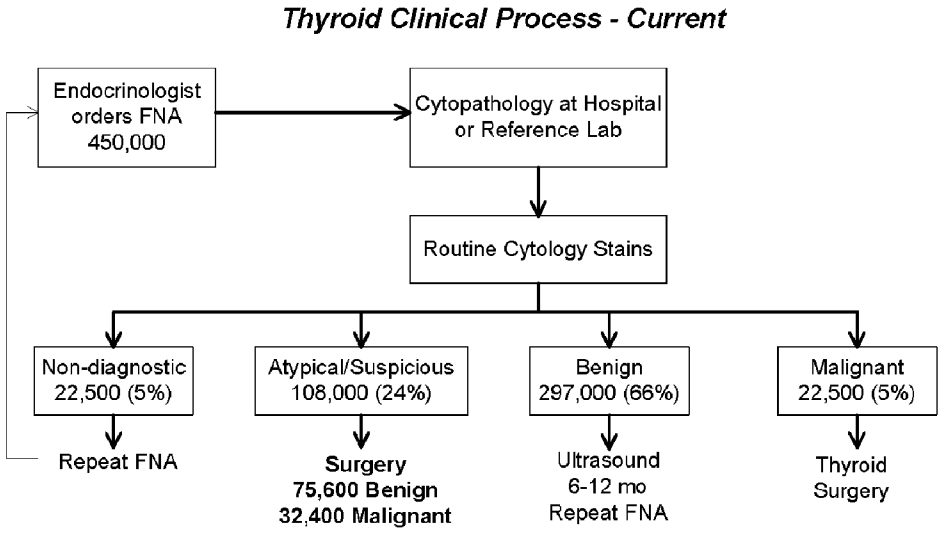

100
Sample
105
Non Diagnostic
110
Benign
115
Ambiguous/ Suspicious Indeterminant
120
Malignant
125
Routine Cytological Stains
130
Molecular Profiling
135
Benign Diagnosis
140
Malignant Diagnosis

Figure 18A


Thyroid Clinical Process - Current
Endocrinologist orders FNA 450,000
Cytopathology at Hospital or Reference Lab
Routine Cytology Stains
Non-diagnostic 22,500 (5%)
Atypical/Suspicious 108,000 (24%)
Benign 297,000 (66%)
Malignant 22,500 (5%)
Repeat FNA
Surgery 75,600 Benign 32,400 Malignant
Ultrasound 6-12 mo Repeat FNA
Thyroid Surgery
Three quarters of surgeries on nodules with Atypical or Suspicious cytology are potentially avoidable.

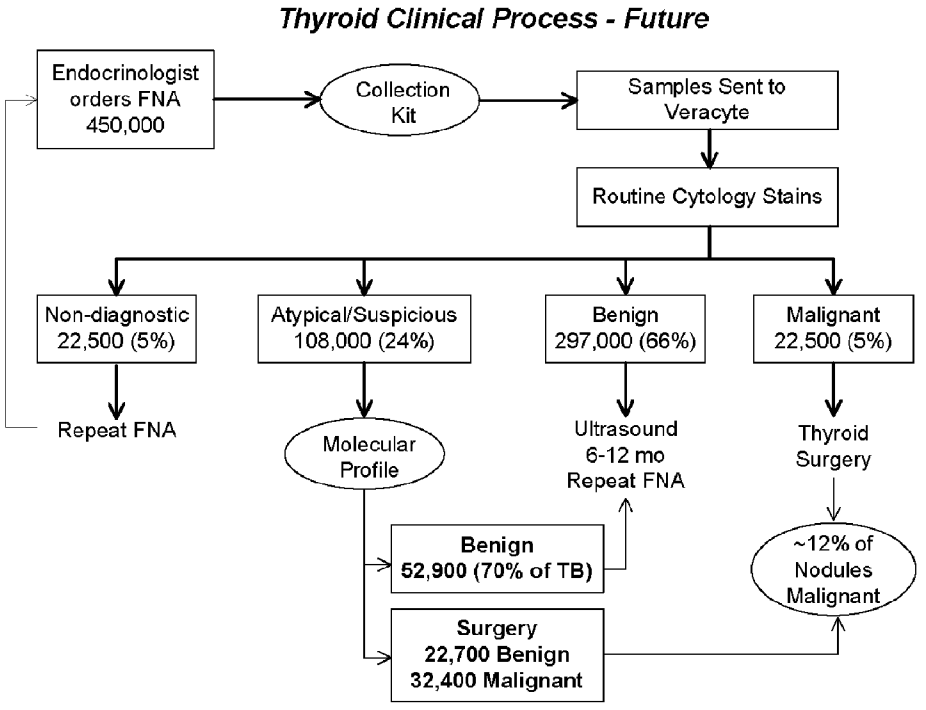

Thyroid Clinical Process - Future
Endocrinologist orders FNA 450,000
Collection Kit
Samples Sent to Veracyte
Routine Cytology Stains
Non-diagnostic 22,500 (5%)
Atypical/Suspicious 108,000 (24%)
Benign 297,000 (66%)
Malignant 22,500 (5%)
Repeat FNA
Molecular Profile
Ultrasound 6-12 mo Repeat FNA
Thyroid Surgery
Benign 52,900 (70% of TB)
~12% of Nodules Malignant
Surgery 22,700 Benign 32,400 Malignant

Figure 18B

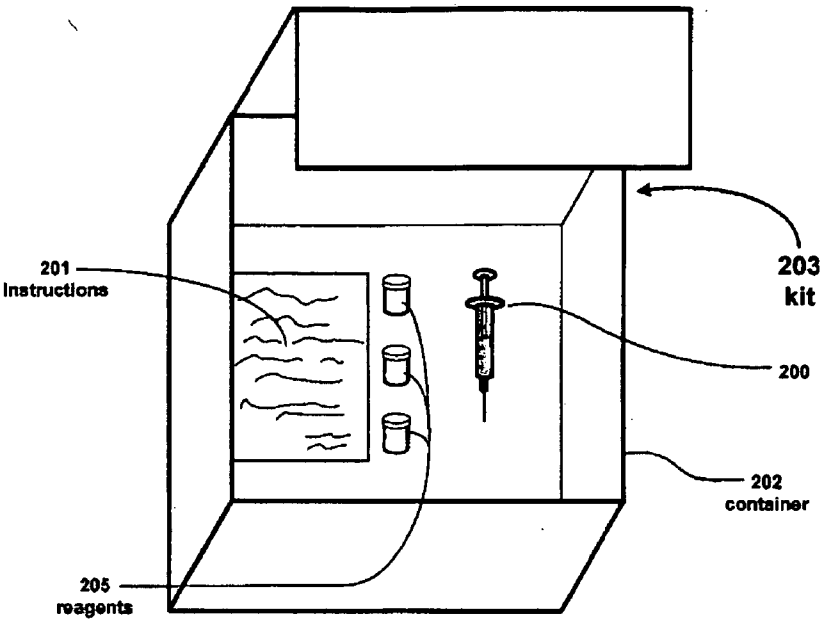


Figure 19

Molecular Profiling Report

Customer: 1234

Tissue Type: thyroid

Preliminary Diagnosis: nodule

Sample Quality: ++

Nodule ID	Benign	Not Benign	Non Diagnostic
a	+	-	-
b	+	-	-
c	+	-	-
d	+	-	-

Figure 20

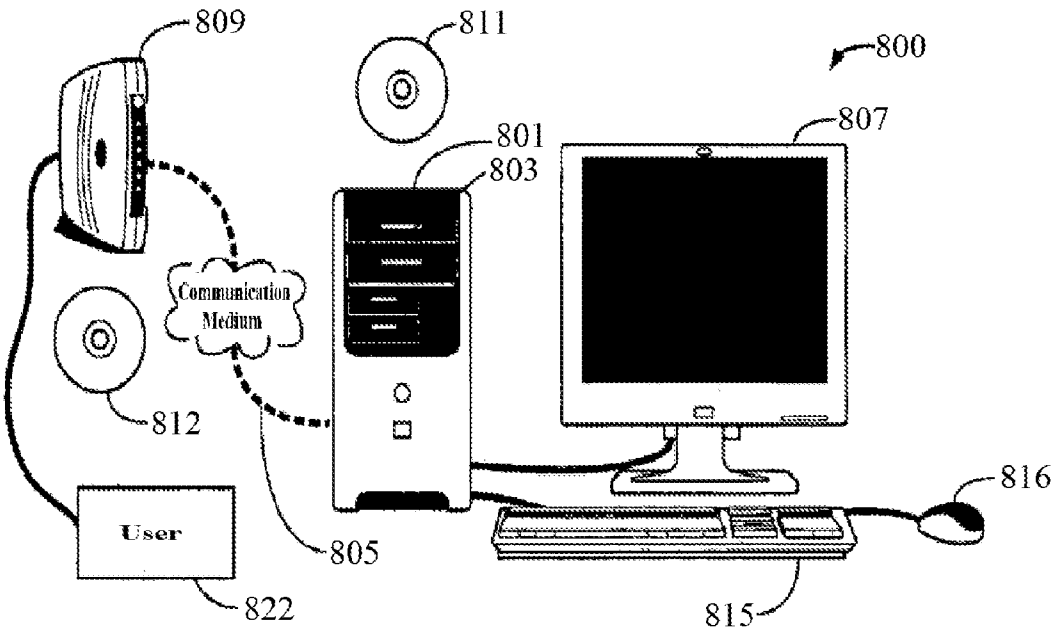

809
811
800
807
801
803
Communication Medium
812
User
805
816
822
815

Figure 21

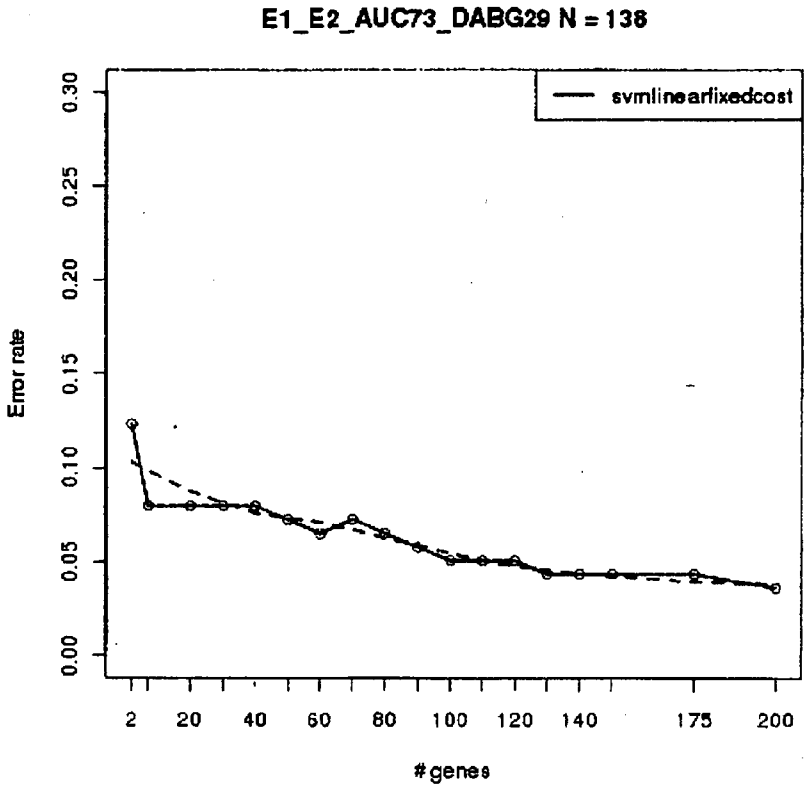

E1_E2_AUC73_DABG29 N = 138
svmlinearfixedcost
Error rate
0.00
0.05
0.10
0.15
0.20
0.25
0.30
2
20
40
60
80
100
120
140
175
200
genes

Figure 22

METHODS AND COMPOSITIONS OF MOLECULAR PROFILING FOR DISEASE DIAGNOSTICS

CROSS REFERENCE

[0001] This application is a continuation of U.S. patent application Ser. No. 13/589,022, filed on Aug. 17, 2012, which is a continuation of U.S. patent application Ser. No. 12/592,065, filed on Nov. 17, 2009, which claims the benefit of U.S. Provisional Application No. 61/199,585, entitled "Methods and Compositions of Molecular Profiling for Diagnosis of Cancer" filed Nov. 17, 2008, and U.S. Provisional Application No. 61/270,812, entitled "Methods and Compositions of Molecular Profiling for Diagnosis of Cancer" filed Jul. 13, 2009, each of which is incorporated herein by reference in its entirety.

BACKGROUND OF THE INVENTION

[0002] Cancer is the second leading cause of death in the United States and one of the leading causes of mortality worldwide. Nearly 25 million people are currently living with cancer, with 11 million new cases diagnosed each year. Furthermore, as the general population continues to age, cancer will become a bigger and bigger problem. The World Health Organization projects that by the year 2020, global cancer rates will increase by 50%.

[0003] Successful treatment of cancer starts with early and accurate diagnosis. Current methods of diagnosis include cytological examination of tissue samples taken by biopsy or imaging of tissues and organs for evidence of aberrant cellular proliferation. While these techniques have proven to be both useful and inexpensive, they suffer from a number of drawbacks. First, cytological analysis and imaging techniques for cancer diagnosis often require a subjective assessment to determine the likelihood of malignancy. Second, the increased use of these techniques has lead to a sharp increase in the number of indeterminate results in which no definitive diagnosis can be made. Third, these routine diagnostic methods lack a rigorous method for determining the probability of an accurate diagnosis. Fourth, these techniques may be incapable of detecting a malignant growth at very early stages. Fifth, these techniques do not provide information regarding the basis of the aberrant cellular proliferation.

[0004] Many of the newer generation of treatments for cancer, while exhibiting greatly reduced side effects, are specifically targeted to a certain metabolic or signaling pathway, and will only be effective against cancers that are reliant on that pathway. Further, the cost of any treatments can be prohibitive for an individual, insurance provider, or government entity. This cost could be at least partially offset by improved methods that accurately diagnose cancers and the pathways they rely on at early stages. These improved methods would be useful both for preventing unnecessary therapeutic interventions as well as directing treatment.

[0005] In the case of thyroid cancer it is estimated that out of the approximately 130,000 thyroid removal surgeries performed each year due to suspected malignancy in the United States, only about 54,000 are necessary. Thus, approximately 76,000 unnecessary surgeries are performed annually. In addition, there are continued treatment costs and complications due to the need for lifelong drug therapy to replace the lost thyroid function. Accordingly, there is a need for improved testing modalities and business practices that improve upon current methods of cancer diagnosis.

[0006] The thyroid has at least two kinds of cells that make hormones. Follicular cells make thyroid hormone, which affects heart rate, body temperature, and energy level. C cells make cacitonin, a hormone that helps control the level of calcium in the blood. Abnormal growth in the thyroid can result in the formation of nodules, which can be either benign or malignant. Thyroid cancer includes at least four different kinds of malignant tumors of the thyroid gland: papillary, follicular, medullary and anaplastic.

SUMMARY OF THE INVENTION

[0007] The present invention includes a method for diagnosing thyroid disease in a subject, the method comprising (a) providing a nucleic acid sample from a subject; (b) detecting the amount of one or more genes, gene products, or transcripts selected from the group consisting of the genes or transcripts listed in Tables 2 or their complement; and (c) determining whether said subject has or is likely to have a malignant or benign thyroid condition based on the results of step (b).

[0008] The present invention also includes a composition comprising one or more binding agents that specifically bind to the one or more polymorphisms selected from the group consisting of the polymorphisms listed in Tables.

INCORPORATION BY REFERENCE

[0009] All publications and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:

[0011] FIG. **1** is a table listing 75 thyroid samples examined for gene expression analysis using the Affymetrix Human Exon 10ST array to identify genes that are significantly differentially expressed or alternatively spliced between malignant, benign, and normal samples. The name for each sample and the pathological classification is listed.

[0012] FIG. **2** is a table listing the top 100 differentially expressed genes at the gene level. Data are from the dataset in which benign malignant and normal thyroid samples were compared at the gene level. Markers were selected based on statistical significance after Benjamini and Hochberg correction for false discover rate (FDR). Positive numbers denote up regulation and negative numbers denote down regulation of expression.

[0013] FIG. **3** is a table listing the top 100 alternatively spliced genes. Data are from the dataset in which benign malignant and normal thyroid samples were compared at the gene level. Markers were selected based on statistical significance after Benjamini and Hochberg correction for false discovery rate (FDR).

[0014] FIG. **4** is a table listing the top 100 differentially expressed genes at the probe-set level. Data were from the Probe-set dataset. Positive numbers denote up-regulation of gene expression, while negative numbers denote down regulation.

[0015] FIG. **5** is a table listing the top 100 significant diagnostic markers determined by gene level analysis. Markers in this list show both differential gene expression and alternative exon splicing. Positive numbers denote up-regulation, while negative numbers denote down regulation. This table lists 3-sets of calculated fold-changes for any given marker to allow comparison between the groups malignant vs. benign, benign, versus normal, and malignant versus normal.

[0016] FIG. **6** is a table listing the genes identified as contributing to thyroid cancer diagnosis by molecular profiling of gene expression levels and/or alternative exon splicing. Markers identified from the dataset in which benign, malignant and normal samples were analyzed at the gene level are referred to as BMN in the data source column; and likewise, markers identified from dataset in which the benign and malignant samples were analyzed at the gene level are referred to as BM in the data source column. Similarly, markers identified at the probe-set level from the dataset in which benign, and malignant samples were analyzed are referred to as Probe-set in the data source column.

[0017] FIG. **7** is a table listing tissue samples examined for gene expression analysis. The samples were classified by pathological analysis as benign (B) or malignant (M). Benign samples were further classified as follicular adenoma (FA), lymphocytic thyroiditis (LCT), or nodular hyperplasia (NHP). Malignant samples were further classified as Hurthle cell carcinoma (HC), follicular carcinoma (FC), follicular variant of pappillary thyroid carcinoma (FVPTC), papillary thyroid carcinoma (PTC), medullary thyroid carcinoma (MTC), or anaplastic carcinoma (ATC).

[0018] FIG. **8** is a table listing fine needle aspirate samples examined for gene expression analysis. The samples were classified by pathological analysis as benign (B) or malignant (M). Benign samples were further classified as follicular adenoma (FA), lymphocytic thyroiditis (LCT), Hurthle cell adenoma (HA), or nodular hyperplasia (NHP). Malignant samples were further classified as Hurthle cell carcinoma (HC), follicular carcinoma (FC), follicular variant of pappillary thyroid carcinoma (FVPTC), papillary thyroid carcinoma (PTC), medullary thyroid carcinoma (MTC), or anaplastic carcinoma (ATC).

[0019] FIG. **9** is a table listing genes identified from expression analysis of the tissue samples listed in FIG. **7** which exhibit significant differences in expression between malignant and benign samples as determined by feature selection using LIMMA (linear models for micro array data) and SVM (support vector machine) for classification of malignant vs. benign samples. Rank denotes the marker significance (lower rank, higher significance) after Benjamini and Hochberg correction for False Discovery Rate (FDR). Gene symbol denotes the name of the gene. TCID denotes the transcript cluster ID of the gene used in the Affymetrix Human Exon 10ST array. Ref Seq denotes the name of the corresponding reference sequence for that gene. The column labeled "Newly Discovered Marker" denotes gene expression markers which have not previously been described as differentially expressed in malignant vs. benign thyroid tissues.

[0020] FIG. **10** is a table listing genes identified from expression analysis of the tissue samples listed in FIG. **8** which exhibit significant differences in expression between medullary thyroid carcinoma (MTC) and other pathologies as determined by feature selection using LIMMA (linear models for micro array data) and SVM (support vector machine) for classification of MTC vs. other samples. Rank denotes the marker significance (lower rank, higher significance) after Benjamini and Hochberg correction for False Discovery Rate (FDR). Gene symbol denotes the name of the gene. TCID denotes the transcript cluster ID of the gene used in the Affymetrix Human Exon 10ST array. P value indicates the statistical significance of the differential expression between MTC and non-MTC samples. Fold Change indicates the degree of differential expression between MTC and non-MTC samples. The column labeled "Newly Discovered Marker" denotes gene expression markers which have not previously been described as differentially expressed in malignant vs. benign thyroid tissues.

[0021] FIG. **11** is a table listing genes identified from expression analysis of the samples listed in FIGS. **7** and **8** which exhibit significant differences in expression between benign and malignant samples as determined by a repeatability based meta-analysis classification algorithm.

[0022] FIG. **12** is a table listing genes identified from expression analysis of the samples listed in FIGS. **7** and **8** which exhibit significant (posterior probability >0.9) differences in expression between benign and malignant samples as determined by Bayesian ranking of the differentially expressed genes. deriving type I and type II error rates from previously published studies to determine prior probabilities, combining these prior probabilities with the output of the dataset derived from expression analysis of the samples listed in FIG. **10** to estimate posterior probabilities of differential gene expression, and then combining the results of the expression analysis of the samples listed in FIG. **11** with the estimated posterior probabilities to calculate final posterior probabilities of differential gene expression. These posterior probabilities were then used to rank the differentially expressed genes.

[0023] FIG. **13** is a table listing genes identified from expression analysis of the samples listed in FIG. **7** which exhibit differential expression between samples categorized as FA, LCT, NHP, HC, FC, FVPTC, PTC, MTC, or ATC as determined by feature selection using LIMMA (linear models for micro array data) and SVM (support vector machine) for classification.

[0024] FIG. **14** is a table listing fine needle aspirate samples examined for micro RNA (miRNA) expression analysis using an Agilent Human v2 miRNA microarray chip. The samples were classified by pathological analysis as benign (B) or malignant (M). Benign samples were further classified as follicular adenoma (FA), or nodular hyperplasia (NHP). Malignant samples were further classified as follicular carcinoma (FC), follicular variant of pappillary thyroid carcinoma (FVPTC), papillary thyroid carcinoma (PTC), or medullary thyroid carcinoma (MTC).

[0025] FIG. **15** is a table listing fine needle aspirate samples examined for micro RNA (miRNA) expression analysis using an Illumina Human v2 miRNA array. The samples were classified by pathological analysis as benign (B), non diagnostic, or malignant (M). Benign samples were further classified as benign nodule (BN), follicular neoplasm

(FN), (LCT), or (NHP). Malignant samples were further classified as (FVPTC), or (PTC).

[0026] FIG. **16** is a table listing micro RNAs (miRNAs) identified from analysis of the samples listed in FIG. **14** which exhibit differential expression between samples categorized as benign or malignant. The miRNA column denotes the name of the miRNA. The CHR column denotes the chromosome the miRNA is located on. The P column denotes the statistical confidence or p-value provided by the analysis. The DE column denotes whether the listed miRNA is upregulated (1) in malignant samples or downregulated (−1) in malignant samples. The patent column denotes any patents or applications that describe these miRNAs.

[0027] FIG. **17** is a table listing micro RNAs (miRNAs) identified from analysis of the samples listed in FIG. **15** which exhibit differential expression between samples categorized as benign or malignant. The miRNA column denotes the name of the miRNA. The probe ID column denotes the corresponding probe ID in the illumina array. The CHR column denotes the chromosome the miRNA is located on. The P column denotes the statistical confidence or p-value provided by the analysis. The DE column denotes whether the listed miRNA is upregulated (no sign) in malignant samples or downregulated (negative sign) in malignant samples. The Rep column denotes the repeatability score provided by a "hot probes" type analysis of the hybridization data. The patent column denotes any patents or applications that describe these miRNAs.

[0028] FIGS. **18**A and **18**B are flow charts describing how molecular profiling may be used to improve the accuracy of routine cytological examination. FIG. **18**A and FIG. **18**B describe alternate embodiments of the molecular profiling business.

[0029] FIG. **19** is an illustration of a kit provided by the molecular profiling business.

[0030] FIG. **20** is an illustration of a molecular profiling results report.

[0031] FIG. **21** depicts a computer useful for displaying, storing, retrieving, or calculating diagnostic results from the molecular profiling; displaying, storing, retrieving, or calculating raw data from genomic or nucleic acid expression analysis; or displaying, storing, retrieving, or calculating any sample or customer information useful in the methods of the present invention.

[0032] FIG. **22** depicts a titration curve of error rate vs. number of genes using an SVM-based classification algorithm. The titration curve plateaus when the classification algorithm examines 200-250 genes. These data indicate that the overall error rate of the current algorithm was 4% (5/138).

DETAILED DESCRIPTION OF THE INVENTION

I. Introduction

[0033] The present disclosure provides novel methods for diagnosing abnormal cellular proliferation from a biological test sample, and related kits and compositions. The present invention also provides methods and compositions for differential diagnosis of types of aberrant cellular proliferation such as carcinomas including follicular carcinomas (FC), follicular variant of papillary thyroid carcinomas (FVPTC), Hurthle cell carcinomas (HC), Hurthle cell adenomas (HA); papillary thyroid carcinomas (PTC), medullary thyroid carcinomas (MTC), and anaplastic carcinomas (ATC); adenomas including follicular adenomas (FA); nodule hyperplasias (NHP); colloid nodules (CN); benign nodules (BN); follicular neoplasms (FN); lymphocytic thyroiditis (LCT), including lymphocytic autoimmune thyroiditis; parathyroid tissue; renal carcinoma metastasis to the thyroid; melanoma metastasis to the thyroid; B-cell lymphoma metastasis to the thyroid; breast carcinoma to the thyroid; benign (B) tumors, malignant (M) tumors, and normal (N) tissues. The present invention further provides novel markers including microRNAs (miRNAs) and gene expression product markers and novel groups of genes and markers useful for the diagnosis, characterization, and treatment of cellular proliferation. Additionally the present invention provides business methods for providing enhanced diagnosis, differential diagnosis, monitoring, and treatment of cellular proliferation.

[0034] Cancer is a leading cause of death in the United States. Early and accurate diagnosis of cancer is critical for effective management of this disease. It is therefore important to develop testing modalities and business practices to enable cancer diagnosis that is more accurately and earlier. Expression product profiling, also referred to as molecular profiling, provides a powerful method for early and accurate diagnosis of tumors or other types of cancers from a biological sample.

[0035] Typically, screening for the presence of a tumor or other type of cancer, involves analyzing a biological sample taken by various methods such as, for example, a biopsy. The biological sample is then prepared and examined by one skilled in the art. The methods of preparation can include but are not limited to various cytological stains, and immunohistochemical methods. Unfortunately, traditional methods of cancer diagnosis suffer from a number of deficiencies. These deficiencies include: 1) the diagnosis may require a subjective assessment and thus be prone to inaccuracy and lack of reproducibility, 2) the methods may fail to determine the underlying genetic, metabolic or signaling pathways responsible for the resulting pathogenesis, 3) the methods may not provide a quantitative assessment of the test results, and 4) the methods may be unable to provide an unambiguous diagnosis for certain samples.

[0036] One hallmark of cancer is dysregulation of normal transcriptional control leading to aberrant expression of genes or other RNA transcripts such as miRNAs. Among the aberrantly expressed transcripts are genes involved in cellular transformation, for example tumor suppressors and oncogenes. Tumor suppressor genes and oncogenes may be up-regulated or down-regulated in tumors when compared to normal tissues. Known tumor suppressors and oncogenes include, but are not limited to brca1, brca2, bcr-ab1, bcl-2, HER2, N-myc, C-myc, BRAF, RET, Ras, KIT, Jun, Fos, and p53. This abnormal expression may occur through a variety of different mechanisms. It is not necessary in the present invention to understand the mechanism of aberrant expression, or the mechanism by which carcinogenesis occurs. Nevertheless, finding a marker or set of markers whose expression is up or down regulated in a sample as compared to a normal sample may be indicative of cancer. Furthermore, the particular aberrantly expressed markers or set of markers may be indicative of a particular type of cancer, or even a recommended treatment protocol. Additionally the methods of the present invention are not meant to be limited solely to canonically defined tumor suppressors or onco-

genes. Rather, it is understood that any marker, gene or set of genes or markers that is determined to have a statistically significant correlation with respect to expression level or alternative gene splicing to a benign, malignant, or normal diagnosis is encompassed by the present invention.

[0037] In one embodiment, the methods of the present invention seek to improve upon the accuracy of current methods of cancer diagnosis. Improved accuracy can result from the measurement of multiple genes and/or expression markers, the identification of gene expression products such as miRNAs, rRNA, tRNA and mRNA gene expression products with high diagnostic power or statistical significance, or the identification of groups of genes and/or expression products with high diagnostic power or statistical significance, or any combination thereof.

[0038] For example, increased expression of a number of receptor tyrosine kinases has been implicated in carcinogenesis. Measurement of the gene expression product level of a particular receptor tyrosine kinase known to be differentially expressed in cancer cells may provide incorrect diagnostic results leading to a low accuracy rate. Measurement of a plurality of receptor tyrosine kinases may increase the accuracy level by requiring a combination of alternate expressed genes to occur. In some cases, measurement of a plurality of genes might therefore increase the accuracy of a diagnosis by reducing the likelihood that a sample may exhibit an aberrant gene expression profile by random chance.

[0039] Similarly, some gene expression products within a group such as receptor tyrosine kinases may be indicative of a disease or condition when their expression levels are higher or lower than normal. The measurement of expression levels of other gene products within that same group may provide diagnostic utility. Thus, in one embodiment, the invention measures two or more gene expression products that are within a group. For example, in some embodiments, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45 or 50 gene expression products are measured from a group. Various groups are defined within the specification, such as groups useful for diagnosis of subtypes of thyroid cancer or groups of gene expression products that fall within particular ontology groups. In another embodiment, it would be advantageous to measure the expression levels of sets of genes that accurately indicate the presence or absence of cancer from multiple groups. For example, the invention contemplates the use of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45 or 50 gene expression groups, each with 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45 or 50 gene expression products measured.

[0040] Additionally, increased expression of other oncogenes such as for example Ras in a biological sample may also be indicative of the presence of cancerous cells. In some cases, it may be advantageous to determine the expression level of several different classes of oncogenes such as for example receptor tyrosine kinases, cytoplasmic tyrosine kinases, GTPases, serine/threonine kinases, lipid kinases, mitogens, growth factors, and transcription factors. The determination of expression levels and/or exon usage of different classes or groups of genes involved in cancer progression may in some cases increase the diagnostic power of the present invention.

[0041] Groups of expression markers may include markers within a metabolic or signaling pathway, or genetically or functionally homologous markers. For example, one group of markers may include genes involved in the epithelial growth factor signaling pathway. Another group of markers may include mitogen-activated protein kinases. The present invention also provides methods and compositions for detecting (i.e. measuring) measuring gene expression markers from multiple and/or independent metabolic or signaling pathways.

[0042] In one embodiment, expression product markers of the present invention may provide increased accuracy of cancer diagnosis through the use of multiple expression product markers and statistical analysis. In particular, the present invention provides, but is not limited to, RNA expression profiles associated with thyroid cancers. The present invention also provides methods of characterizing thyroid tissue samples, and kits and compositions useful for the application of said methods. The disclosure further includes methods for running a molecular profiling business.

[0043] The present disclosure provides methods and compositions for improving upon the current state of the art for diagnosing cancer.

[0044] In some embodiments, the present invention provides a method of diagnosing cancer comprising the steps of: obtaining a biological sample comprising gene expression products; determining the expression level for one or more gene expression products of the biological sample; and identifying the biological sample as cancerous wherein the gene expression level is indicative of the presence of thyroid cancer in the biological sample. This can be done by correlating the gene expression levels with the presence of thyroid cancer in the biological sample. In one embodiment, the gene expression products are selected from FIG. **6**. In some embodiments, the method further comprises the step of comparing the expression level of the one or more gene expression products to a control expression level for each gene expression product in a control sample, wherein the biological sample is identified as cancerous if there is a difference in the gene expression level between a gene expression product in the biological sample and the control sample.

[0045] In some embodiments, the present invention provides a method of diagnosing cancer comprising the steps of: obtaining a biological sample comprising alternatively spliced gene expression products; determining the expression level for one or more gene expression products of the biological sample; and identifying the biological sample as cancerous wherein the gene expression level is indicative of the presence of thyroid cancer in the biological sample. This can be done by correlating the gene expression levels with the presence of thyroid cancer in the biological sample. In one embodiment, the alternatively spliced gene expression products are selected from FIG. **6**, wherein the differential gene expression product alternative exon usage is compared between the biological sample and a control sample; and identifying the biological sample as cancerous if there is a difference in gene expression product alternative exon usage between the biological sample and the control sample at a specified confidence level. In some embodiments, the genes selected from FIG. **6** are further selected from genes listed in FIG. **2**, FIG. **3**, FIG. **4**, or FIG. **5**.

[0046] In some embodiments, the present invention provides a method of diagnosing cancer that gives a specificity or sensitivity that is greater than 70% using the subject methods described herein, wherein the gene expression product levels are compared between the biological sample

and a control sample; and identifying the biological sample as cancerous if there is a difference in the gene expression levels between the biological sample and the control sample at a specified confidence level. In some embodiments, the specificity and/or sensitivity of the present method is at least 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more.

[0047] In some embodiments, the nominal specificity is greater than or equal to 70%. The nominal negative predictive value (NPV) is greater than or equal to 95%. In some embodiments, the NPV is at least 95%, 95.5%, 96%, 96.5%, 97%, 97.5%, 98%, 98.5%, 99%, 99.5% or more.

[0048] Sensitivity typically refers to TP/(TP+FN), where TP is true positive and FN is false negative. Number of Continued Indeterminate results divided by the total number of malignant results based on adjudicated histopathology diagnosis. Specificity typically refers to TN/(TN+FP), where TN is true negative and FP is false positive. The number of benign results divided by the total number of benign results based on adjudicated histopathology diagnosis. Positive Predictive Value (PPV): TP/(TP+FP); Negative Predictive Value (NPV): TN/(TN+FN).

[0049] Marker panels are chosen to accommodate adequate separation of benign from non-benign expression profiles. Training of this multi-dimensional classifier, i.e., algorithm, was performed on over 500 thyroid samples, including >300 thyroid FNAs. Many training/test sets were used to develop the preliminary algorithm. An exemplary data set is shown in FIG. **22**. First the overall algorithm error rate is shown as a function of gene number for benign vs non-benign samples. All results are obtained using a support vector machine model which is trained and tested in a cross-validated mode (30-fold) on the samples.

[0050] In some embodiments, the difference in gene expression level is at least 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45% or 50% or more. In some embodiments, the difference in gene expression level is at least 2, 3, 4, 5, 6, 7, 8, 9, 10 fold or more. In some embodiments, the biological sample is identified as cancerous with an accuracy of greater than 75%, 80%, 85%, 90%, 95%, 99% or more. In some embodiments, the biological sample is identified as cancerous with a sensitivity of greater than 95%. In some embodiments, the biological sample is identified as cancerous with a specificity of greater than 95%. In some embodiments, the biological sample is identified as cancerous with a sensitivity of greater than 95% and a specificity of greater than 95%. In some embodiments, the accuracy is calculated using a trained algorithm.

[0051] In some embodiments, the present invention provides gene expression products corresponding to genes selected from Table 3, Table 4 and/or Table 5.

[0052] In some embodiments, the present invention provides a method of diagnosing cancer comprising using gene expression products from one or more of the following signaling pathways. The signaling pathways from which the genes can be selected include but are not limited to: acute myeloid leukemia signaling, somatostatin receptor 2 signaling, cAMP-mediated signaling, cell cycle and DNA damage checkpoint signaling, G-protein coupled receptor signaling, integrin signaling, melanoma cell signaling, relaxin signaling, and thyroid cancer signaling. In some embodiments, more than one gene is selected from a single signaling pathway to determine and compare the differential gene expression product level between the biological sample and a control sample. Other signaling pathways include, but are not limited to, an adherens, ECM, thyroid cancer, focal adhesion, apoptosis, p53, tight junction, TGFbeta, ErbB, Wnt, pathways in cancer overview, cell cycle, VEGF, Jak/STAT, MAPK, PPAR, mTOR or autoimmune thyroid pathway. In other embodiments, at least two genes are selected from at least two different signaling pathways to determine and compare the differential gene expression product level between the biological sample and the control sample. Methods and compositions of the invention can have genes selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50 or more signaling pathways and can have from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50 or more gene expression products from each signaling pathway, in any combination. In some embodiments, the set of genes combined give a specificity or sensitivity of greater than 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 99.5%, or a positive predictive value or negative predictive value of at least 95%, 95.5%, 96%, 96.5%, 97%, 97.5%, 98%, 98.5%, 99%, 99.5% or more.

[0053] In some embodiments, the present invention provides a method of diagnosing cancer comprising genes selected from at least two different ontology groups. In some embodiments, the ontology groups from which the genes can be selected include but are not limited to: cell aging, cell cortex, cell cycle, cell death/apoptosis, cell differentiation, cell division, cell junction, cell migration, cell morphogenesis, cell motion, cell projection, cell proliferation, cell recognition, cell soma, cell surface, cell surface linked receptor signal transduction, cell adhesion, transcription, immune response, or inflammation. In some embodiments, more than one gene is selected from a single ontology group to determine and compare the differential gene expression product level between the biological sample and a control sample. In other embodiments, at least two genes are selected from at least two different ontology groups to determine and compare the differential gene expression product level between the biological sample and the control sample. Methods and compositions of the invention can have genes selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50 or more gene ontology groups and can have from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50 or more gene expression products from each gene ontology group, in any combination. In some embodiments, the set of genes combined give a specificity or sensitivity of greater than 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 99.5%, or a positive predictive value or negative predictive value of at least 95%, 95.5%, 96%, 96.5%, 97%, 97.5%, 98%, 98.5%, 99%, 99.5% or more.

[0054] In some embodiments, the present invention provides a method of classifying cancer comprising the steps of: obtaining a biological sample comprising gene expression products; determining the expression level for one or more gene expression products of the biological sample that are differentially expressed in different subtypes of a cancer; and identifying the biological sample as cancerous wherein the gene expression level is indicative for a subtype of cancer. In some embodiments, the method further comprises the step of comparing the expression level of the one or more gene expression products to a control expression level for each gene expression product in a control sample, wherein the biological sample is identified as cancerous if there is a

difference in the gene expression level between a gene expression product in the biological sample and the control sample. In some embodiments, the subject methods distinguish follicular carcinoma from medullary carcinoma. In some embodiments, the subject methods distinguish a benign thyroid disease from a malignant thyroid tumor/carcinoma.

[0055] In some embodiments, the gene expression product of the subject methods is a protein, and the amount of protein is compared. The amount of protein can be determined by one or more of the following: ELISA, mass spectrometry, blotting, or immunohistochemistry. RNA can be measured by one or more of the following: microarray, SAGE, blotting, RT-PCR, or quantitative PCR.

[0056] In some embodiments, the difference in gene expression level, for example, mRNA, protein, or alternatively spliced gene product, between a biological sample and a control sample that can be used to diagnose cancer is at least 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 6.5, 7, 7.5, 8, 8.5, 9, 9.5, 10 fold or more.

[0057] In some embodiments, the biological sample is classified as cancerous or positive for a subtype of cancer with an accuracy of greater than 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 99.5%. The diagnosis accuracy as used herein includes specificity, sensitivity, positive predictive value, negative predictive value, and/or false discovery rate.

[0058] When classifying a biological sample for diagnosis of cancer, there are typically four possible outcomes from a binary classifier. If the outcome from a prediction is p and the actual value is also p, then it is called a true positive (TP); however if the actual value is n then it is said to be a false positive (FP). Conversely, a true negative has occurred when both the prediction outcome and the actual value are n, and false negative is when the prediction outcome is n while the actual value is p. In one embodiment, consider a diagnostic test that seeks to determine whether a person has a certain disease. A false positive in this case occurs when the person tests positive, but actually does not have the disease. A false negative, on the other hand, occurs when the person tests negative, suggesting they are healthy, when they actually do have the disease. In some embodiments, ROC curve assuming real-world prevalence of subtypes can be generated by re-sampling errors achieved on available samples in relevant proportions.

[0059] The positive predictive value (PPV), or precision rate, or post-test probability of disease, is the proportion of patients with positive test results who are correctly diagnosed. It is the most important measure of a diagnostic method as it reflects the probability that a positive test reflects the underlying condition being tested for. Its value does however depend on the prevalence of the disease, which may vary. In one example, FP (false positive); TN (true negative); TP (true positive); FN (false negative).

$$\text{False positive rate } (\alpha) = FP/(FP+TN) = \text{specificity}$$

$$\text{False negative rate } (\beta) = FN/(TP+FN) = \text{sensitivity}$$

$$\text{Power} = \text{sensitivity} = 1-\beta$$

$$\text{Likelihood-ratio positive} = \text{sensitivity}/(1-\text{specificity})$$

$$\text{Likelihood-ratio negative} = (1-\text{sensitivity})/\text{specificity}$$

[0060] The negative predictive value is the proportion of patients with negative test results who are correctly diagnosed. PPV and NPV measurements can be derived using appropriate disease subtype prevalence estimates. An estimate of the pooled malignant disease prevalence can be calculated from the pool of indeterminates which roughly classify into B vs M by surgery. For subtype specific estimates, in some embodiments, disease prevalence may sometimes be incalculable because there are not any available samples. In these cases, the subtype disease prevalence can be substituted by the pooled disease prevalence estimate.

[0061] In some embodiments, the level of expression products or alternative exon usage is indicative of one of the following: follicular cell carcinoma, anaplastic carcinoma, medullary carcinoma, or sarcoma. In some embodiments, the one or more genes selected using the methods of the present invention for diagnosing cancer contain representative sequences corresponding to a set of metabolic or signaling pathways indicative of cancer.

[0062] In some embodiments, the results of the expression analysis of the subject methods provide a statistical confidence level that a given diagnosis is correct. In some embodiments, such statistical confidence level is above 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 99.5%.

[0063] In another aspect, the present invention provides a composition for diagnosing cancer comprising oligonucleotides comprising a portion of one or more of the genes listed in FIG. **6** or their complement, and a substrate upon which the oligonucleotides are covalently attached. The composition of the present invention is suitable for use in diagnosing cancer at a specified confidence level using a trained algorithm. In one example, the composition of the present invention is used to diagnose thyroid cancer.

[0064] In one aspect of the present disclosure, samples that have been processed by a cytological company, subjected to routine methods and stains, diagnosed and categorized, are then subjected to molecular profiling as a second diagnostic screen. This second diagnostic screen enables: 1) a significant reduction of false positives and false negatives, 2) a determination of the underlying genetic, metabolic, or signaling pathways responsible for the resulting pathology, 3) the ability to assign a statistical probability to the accuracy of the diagnosis, 4) the ability to resolve ambiguous results, and 5) the ability to distinguish between sub-types of cancer.

[0065] For example, in the specific case of thyroid cancer, molecular profiling of the present invention may further provide a diagnosis for the specific type of thyroid cancer (e.g. papillary, follicular, medullary, or anaplastic). The results of the molecular profiling may further allow one skilled in the art, such as a scientist or medical professional to suggest or prescribe a specific therapeutic intervention. Molecular profiling of biological samples may also be used to monitor the efficacy of a particular treatment after the initial diagnosis. It is further understood that in some cases, molecular profiling may be used in place of, rather than in addition to, established methods of cancer diagnosis.

[0066] In one aspect, the present invention provides algorithms and methods that can be used for diagnosis and monitoring of a genetic disorder. A genetic disorder is an illness caused by abnormalities in genes or chromosomes. While some diseases, such as cancer, are due in part to

genetic disorders, they can also be caused by environmental factors. In some embodiments, the algorithms and the methods disclosed herein are used for diagnosis and monitoring of a cancer such as thyroid cancer.

[0067] Genetic disorders can be typically grouped into two categories: single gene disorders and multifactorial and polygenic (complex) disorders. A single gene disorder is the result of a single mutated gene. There are estimated to be over 4000 human diseases caused by single gene defects. Single gene disorders can be passed on to subsequent generations in several ways. There are several types of inheriting a single gene disorder including but not limited to autosomal dominant, autosomal recessive, X-linked dominant, X-linked recessive, Y-linked and mitochondrial inheritance. Only one mutated copy of the gene will be necessary for a person to be affected by an autosomal dominant disorder. Examples of autosomal dominant type of disorder include but are not limited to Huntington's disease, Neurofibromatosis 1, Marfan Syndrome, Hereditary nonpolyposis colorectal cancer, and Hereditary multiple exostoses. In autosomal recessive disorder, two copies of the gene must be mutated for a person to be affected by an autosomal recessive disorder. Examples of this type of disorder include but are not limited to cystic fibrosis, sickle-cell disease (also partial sickle-cell disease), Tay-Sachs disease, Niemann-Pick disease, spinal muscular atrophy, and dry earwax. X-linked dominant disorders are caused by mutations in genes on the X chromosome. Only a few disorders have this inheritance pattern, with a prime example being X-linked hypophosphatemic rickets. Males and females are both affected in these disorders, with males typically being more severely affected than females. Some X-linked dominant conditions such as Rett syndrome, Incontinentia Pigmenti type 2 and Aicardi Syndrome are usually fatal in males either in utero or shortly after birth, and are therefore predominantly seen in females. X-linked recessive disorders are also caused by mutations in genes on the X chromosome. Examples of this type of disorder include but are not limited to Hemophilia A, Duchenne muscular dystrophy, red-green color blindness, muscular dystrophy and Androgenetic alopecia. Y-linked disorders are caused by mutations on the Y chromosome. Examples include but are not limited to Male Infertility and hypertrichosis pinnae. Mitochondrial inheritance, also known as maternal inheritance, applies to genes in mitochondrial DNA. An example of this type of disorder is Leber's Hereditary Optic Neuropathy.

[0068] Genetic disorders may also be complex, multifactorial or polygenic, this means that they are likely associated with the effects of multiple genes in combination with lifestyle and environmental factors. Although complex disorders often cluster in families, they do not have a clear-cut pattern of inheritance. This makes it difficult to determine a person's risk of inheriting or passing on these disorders. Complex disorders are also difficult to study and treat because the specific factors that cause most of these disorders have not yet been identified. Multifactoral or polygenic disorders that can be diagnosed, characterized and/or monitored using the algorithms and methods of the present invention include but are not limited to heart disease, diabetes, asthma, autism, autoimmune diseases such as multiple sclerosis, cancers, ciliopathies, cleft palate, hypertension, inflammatory bowel disease, mental retardation and obesity.

[0069] Other genetic disorders that can be diagnosed, characterized and/or monitored using the algorithms and methods of the present invention include but are not limited to 1p36 deletion syndrome, 21-hydroxylase deficiency, 22q11.2 deletion syndrome, 47,XYY syndrome, 48, XXXX, 49, XXXXX, aceruloplasminemia, achondrogenesis, type II, achondroplasia, acute intermittent porphyria, adenylosuccinate lyase deficiency, Adrenoleukodystrophy, ALA deficiency porphyria, ALA dehydratase deficiency, Alexander disease, alkaptonuria, alpha-1 antitrypsin deficiency, Alstrom syndrome, Alzheimer's disease (type 1, 2, 3, and 4), Amelogenesis Imperfecta, amyotrophic lateral sclerosis, Amyotrophic lateral sclerosis type 2, Amyotrophic lateral sclerosis type 4, amyotrophic lateral sclerosis type 4, androgen insensitivity syndrome, Anemia, Angelman syndrome, Apert syndrome, ataxia-telangiectasia, Beare-Stevenson cutis gyrata syndrome, Benjamin syndrome, beta thalassemia, biotinidase deficiency, Birt-Hogg-Dube syndrome, bladder cancer, Bloom syndrome, Bone diseases, breast cancer, CADASIL, Camptomelic dysplasia, Canavan disease, Cancer, Celiac Disease, CGD Chronic Granulomatous Disorder, Charcot-Marie-Tooth disease, Charcot-Marie-Tooth disease Type 1, Charcot-Marie-Tooth disease Type 4, Charcot-Marie-Tooth disease, type 2, Charcot-Marie-Tooth disease, type 4, Cockayne syndrome, Coffin-Lowry syndrome, collagenopathy, types II and XI, Colorectal Cancer, Congenital absence of the vas deferens, congenital bilateral absence of vas deferens, congenital diabetes, congenital erythropoietic porphyria, Congenital heart disease, congenital hypothyroidism, Connective tissue disease, Cowden syndrome, Cri du chat, Crohn's disease, fibrostenosing, Crouzon syndrome, Crouzonodermoskeletal syndrome, cystic fibrosis, De Grouchy Syndrome, Degenerative nerve diseases, Dent's disease, developmental disabilities, DiGeorge syndrome, Distal spinal muscular atrophy type V, Down syndrome, Dwarfism, Ehlers-Danlos syndrome, Ehlers-Danlos syndrome arthrochalasia type, Ehlers-Danlos syndrome classical type, Ehlers-Danlos syndrome dermatosparaxis type, Ehlers-Danlos syndrome kyphoscoliosis type, vascular type, erythropoietic protoporphyria, Fabry's disease, Facial injuries and disorders, factor V Leiden thrombophilia, familial adenomatous polyposis, familial dysautonomia, fanconi anemia, FG syndrome, fragile X syndrome, Friedreich ataxia, Friedreich's ataxia, G6PD deficiency, galactosemia, Gaucher's disease (type 1, 2, and 3), Genetic brain disorders, Glycine encephalopathy, Haemochromatosis type 2, Haemochromatosis type 4, Harlequin Ichthyosis, Head and brain malformations, Hearing disorders and deafness, Hearing problems in children, hemochromatosis (neonatal, type 2 and type 3), hemophilia, hepatoerythropoietic porphyria, hereditary coproporphyria, Hereditary Multiple Exostoses, hereditary neuropathy with liability to pressure palsies, hereditary nonpolyposis colorectal cancer, homocystinuria, Huntington's disease, Hutchinson Gilford Progeria Syndrome, hyperoxaluria, primary, hyperphenylalaninemia, hypochondrogenesis, hypochondroplasia, idic15, incontinentia pigmenti, Infantile Gaucher disease, infantile-onset ascending hereditary spastic paralysis, Infertility, Jackson-Weiss syndrome, Joubert syndrome, Juvenile Primary Lateral Sclerosis, Kennedy disease, Klinefelter syndrome, Kniest dysplasia, Krabbe disease, Learning disability, Lesch-Nyhan syndrome, Leukodystrophies, Li-Fraumeni syndrome, lipoprotein lipase deficiency, familial, Male genital disorders, Marfan syndrome, McCune-Albright syn-

drome, McLeod syndrome, Mediterranean fever, familial, MEDNIK, Menkes disease, Menkes syndrome, Metabolic disorders, methemoglobinemia beta-globin type, Methemoglobinemia congenital methaemoglobinaemia, methylmalonic acidemia, Micro syndrome, Microcephaly, Movement disorders, Mowat-Wilson syndrome, Mucopolysaccharidosis (MPS I), Muenke syndrome, Muscular dystrophy, Muscular dystrophy, Duchenne and Becker type, muscular dystrophy, Duchenne and Becker types, myotonic dystrophy, Myotonic dystrophy type 1 and type 2, Neonatal hemochromatosis, neurofibromatosis, neurofibromatosis 1, neurofibromatosis 2, Neurofibromatosis type I, neurofibromatosis type II, Neurologic diseases, Neuromuscular disorders, Niemann-Pick disease, Nonketotic hyperglycinemia, nonsyndromic deafness, Nonsyndromic deafness autosomal recessive, Noonan syndrome, osteogenesis imperfecta (type I and type III), otospondylomegaepiphyseal dysplasia, pantothenate kinase-associated neurodegeneration, Patau Syndrome (Trisomy 13), Pendred syndrome, Peutz-Jeghers syndrome, Pfeiffer syndrome, phenylketonuria, porphyria, porphyria cutanea tarda, Prader-Willi syndrome, primary pulmonary hypertension, prion disease, Progeria, propionic acidemia, protein C deficiency, protein S deficiency, pseudoGaucher disease, pseudoxanthoma elasticum, Retinal disorders, retinoblastoma, retinoblastoma FA—Friedreich ataxia, Rett syndrome, Rubinstein-Taybi syndrome, SADDAN, Sandhoff disease, sensory and autonomic neuropathy type III, sickle cell anemia, skeletal muscle regeneration, Skin pigmentation disorders, Smith Lemli Opitz Syndrome, Speech and communication disorders, spinal muscular atrophy, spinal-bulbar muscular atrophy, spinocerebellar ataxia, spondyloepimetaphyseal dysplasia, Strudwick type, spondyloepiphyseal dysplasia congenita, Stickler syndrome, Stickler syndrome COL2A1, Tay-Sachs disease, tetrahydrobiopterin deficiency, thanatophoric dysplasia, thiamine-responsive megaloblastic anemia with diabetes mellitus and sensorineural deafness, Thyroid disease, Tourette's Syndrome, Treacher Collins syndrome, triple X syndrome, tuberous sclerosis, Turner syndrome, Usher syndrome, variegate porphyria, von Hippel-Lindau disease, Waardenburg syndrome, Weissenbacher-Zweymuller syndrome, Wilson disease, Wolf-Hirschhorn syndrome, Xeroderma Pigmentosum, X-linked severe combined immunodeficiency, X-linked sideroblastic anemia, and X-linked spinal-bulbar muscle atrophy.

[0070] In one embodiment, the subject methods and algorithm are used to diagnose, characterize, and monitor thyroid cancer. Other types of cancer that can be diagnosed, characterized and/or monitored using the algorithms and methods of the present invention include but are not limited to adrenal cortical cancer, anal cancer, aplastic anemia, bile duct cancer, bladder cancer, bone cancer, bone metastasis, central nervous system (CNS) cancers, peripheral nervous system (PNS) cancers, breast cancer, Castleman's disease, cervical cancer, childhood Non-Hodgkin's lymphoma, colon and rectum cancer, endometrial cancer, esophagus cancer, Ewing's family of tumors (e.g. Ewing's sarcoma), eye cancer, gallbladder cancer, gastrointestinal carcinoid tumors, gastrointestinal stromal tumors, gestational trophoblastic disease, hairy cell leukemia, Hodgkin's disease, Kaposi's sarcoma, kidney cancer, laryngeal and hypopharyngeal cancer, acute lymphocytic leukemia, acute myeloid leukemia, children's leukemia, chronic lymphocytic leukemia, chronic myeloid leukemia, liver cancer, lung cancer, lung carcinoid tumors, Non-Hodgkin's lymphoma, male breast cancer, malignant mesothelioma, multiple myeloma, myelodysplastic syndrome, myeloproliferative disorders, nasal cavity and paranasal cancer, nasopharyngeal cancer, neuroblastoma, oral cavity and oropharyngeal cancer, osteosarcoma, ovarian cancer, pancreatic cancer, penile cancer, pituitary tumor, prostate cancer, retinoblastoma, rhabdomyosarcoma, salivary gland cancer, sarcoma (adult soft tissue cancer), melanoma skin cancer, non-melanoma skin cancer, stomach cancer, testicular cancer, thymus cancer, uterine cancer (e.g. uterine sarcoma), vaginal cancer, vulvar cancer, and Waldenstrom's macroglobulinemia.

[0071] In some embodiments, gene expression product markers of the present invention may provide increased accuracy of genetic disorder or cancer diagnosis through the use of multiple gene expression product markers in low quantity and quality, and statistical analysis using the algorithms of the present invention. In particular, the present invention provides, but is not limited to, methods of diagnosing, characterizing and classifying gene expression profiles associated with thyroid cancers. The present invention also provides algorithms for characterizing and classifying thyroid tissue samples, and kits and compositions useful for the application of said methods. The disclosure further includes methods for running a molecular profiling business.

[0072] In one embodiment of the invention, markers and genes can be identified to have differential expression in thyroid cancer samples compared to thyroid benign samples. Illustrative examples having a benign pathology include follicular adenoma, Hurthle cell adenoma, lymphocytic thyroiditis, and nodular hyperplasia. Illustrative examples having a malignant pathology include follicular carcinoma, follicular variant of papillary thyroid carcinoma, medullary carcinoma, and papillary thyroid carcinoma.

[0073] Biological samples may be treated to extract nucleic acid such as DNA or RNA. The nucleic acid may be contacted with an array of probes of the present invention under conditions to allow hybridization. The degree of hybridization may be assayed in a quantitative matter using a number of methods known in the art. In some cases, the degree of hybridization at a probe position may be related to the intensity of signal provided by the assay, which therefore is related to the amount of complementary nucleic acid sequence present in the sample. Software can be used to extract, normalize, summarize, and analyze array intensity data from probes across the human genome or transcriptome including expressed genes, exons, introns, and miRNAs. In some embodiments, the intensity of a given probe in either the benign or malignant samples can be compared against a reference set to determine whether differential expression is occurring in a sample. An increase or decrease in relative intensity at a marker position on an array corresponding to an expressed sequence is indicative of an increase or decrease respectively of expression of the corresponding expressed sequence. Alternatively, a decrease in relative intensity may be indicative of a mutation in the expressed sequence.

[0074] The resulting intensity values for each sample can be analyzed using feature selection techniques including filter techniques which assess the relevance of features by looking at the intrinsic properties of the data, wrapper methods which embed the model hypothesis within a feature

subset search, and embedded techniques in which the search for an optimal set of features is built into a classifier algorithm.

[0075] Filter techniques useful in the methods of the present invention include (1) parametric methods such as the use of two sample t-tests, ANOVA analyses, Bayesian frameworks, and Gamma distribution models (2) model free methods such as the use of Wilcoxon rank sum tests, between-within class sum of squares tests, rank products methods, random permutation methods, or TNoM which involves setting a threshold point for fold-change differences in expression between two datasets and then detecting the threshold point in each gene that minimizes the number of missclassifications (3) and multivariate methods such as bivariate methods, correlation based feature selection methods (CFS), minimum redundancy maximum relevance methods (MRMR), Markov blanket filter methods, and uncorrelated shrunken centroid methods. Wrapper methods useful in the methods of the present invention include sequential search methods, genetic algorithms, and estimation of distribution algorithms. Embedded methods useful in the methods of the present invention include random forest algorithms, weight vector of support vector machine algorithms, and weights of logistic regression algorithms. Bioinformatics. 2007 Oct. 1; 23(19):2507-17 provides an overview of the relative merits of the filter techniques provided above for the analysis of intensity data.

[0076] Selected features may then be classified using a classifier algorithm. Illustrative algorithms include but are not limited to methods that reduce the number of variables such as principal component analysis algorithms, partial least squares methods, and independent component analysis algorithms. Illustrative algorithms further include but are not limited to methods that handle large numbers of variables directly such as statistical methods and methods based on machine learning techniques. Statistical methods include penalized logistic regression, prediction analysis of microarrays (PAM), methods based on shrunken centroids, support vector machine analysis, and regularized linear discriminant analysis. Machine learning techniques include bagging procedures, boosting procedures, random forest algorithms, and combinations thereof. Cancer Inform. 2008; 6: 77-97 provides an overview of the classification techniques provided above for the analysis of microarray intensity data.

[0077] The markers and genes of the present invention can be utilized to characterize the cancerous or non-cancerous status of cells or tissues. The present invention includes a method for diagnosing benign tissues or cells from malignant tissues or cells comprising determining the differential expression of a marker or gene in a thyroid sample of a subject wherein said marker or gene is a marker or gene listed in FIG. **2-6**, **9-13**, **16** or **17**. The present invention also includes methods for diagnosing medullary thyroid carcinoma comprising determining the differential expression of a marker or gene in a thyroid sample of a subject wherein said marker or gene is a marker or gene listed in FIG. **10**. The present invention also includes methods for diagnosing thyroid pathology subtypes comprising determining the differential expression of a marker or gene in a thyroid sample of a subject wherein said marker or gene is a marker or gene listed in FIG. **13**. The present invention also includes methods for diagnosing benign tissues or cells from malignant tissues or cells comprising determining the differential expression of an miRNA in a thyroid sample of a subject wherein said miRNA is an miRNA listed in FIG. **16** or **17**.

[0078] In accordance with the foregoing, the differential expression of a gene, genes, markers, miRNAs, or a combination thereof as disclosed herein may be determined using northern blotting and employing the sequences as identified in herein to develop probes for this purpose. Such probes may be composed of DNA or RNA or synthetic nucleotides or a combination of the above and may advantageously be comprised of a contiguous stretch of nucleotide residues matching, or complementary to, a sequence as identified in FIG. **2-6**, **9-13**, **16** or **17**. Such probes will most usefully comprise a contiguous stretch of at least 15-200 residues or more including 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 175, or 200 nucleotides or more, derived from one or more of the sequences as identified in FIG. **2-6**, **9-13**, **16** or **17**. Thus, where a single probe binds multiple times to the transcriptome of a sample of cells that are cancerous, or are suspected of being cancerous, or predisposed to become cancerous, whereas binding of the same probe to a similar amount of transcriptome derived from the genome of otherwise non-cancerous cells of the same organ or tissue results in observably more or less binding, this is indicative of differential expression of a gene, multiple genes, markers, or miRNAs comprising, or corresponding to, the sequences identified in FIG. **2-6**, **9-13**, **16** or **17** from which the probe sequenced was derived.

[0079] In one such embodiment, the elevated expression, as compared to normal cells and/or tissues of the same organ, is determined by measuring the relative rates of transcription of RNA, such as by production of corresponding cDNAs and then analyzing the resulting DNA using probes developed from the gene sequences as identified in FIG. **2-6**, **9-13**, **16** or **17**. Thus, the levels of cDNA produced by use of reverse transcriptase with the full RNA complement of a cell suspected of being cancerous produces a corresponding amount of cDNA that can then be amplified using polymerase chain reaction, or some other means, such as linear amplification, isothermal amplification, NASB, or rolling circle amplification, to determine the relative levels of resulting cDNA and, thereby, the relative levels of gene expression.

[0080] Increased expression may also be determined using agents that selectively bind to, and thereby detect, the presence of expression products of the genes disclosed herein. For example, an antibody, possibly a suitably labeled antibody, such as where the antibody is bound to a fluorescent or radiolabel, may be generated against one of the polypeptides comprising a sequence as identified in FIGS. **2-6**, and **9-13**, and said antibody will then react with, binding either selectively or specifically, to a polypeptide encoded by one of the genes that corresponds to a sequence disclosed herein. Such antibody binding, especially relative extent of such binding in samples derived from suspected cancerous, as opposed to otherwise non-cancerous, cells and tissues, can then be used as a measure of the extent of expression, or over-expression, of the cancer-related genes identified herein. Thus, the genes identified herein as being over-expressed in cancerous cells and tissues may be over-expressed due to increased copy number, or due to over-

transcription, such as where the over-expression is due to over-production of a transcription factor that activates the gene and leads to repeated binding of RNA polymerase, thereby generating large than normal amounts of RNA transcripts, which are subsequently translated into polypeptides, such as the polypeptides comprising amino acid sequences as identified in FIGS. **2-6**, and **9-13**. Such analysis provides an additional means of ascertaining the expression of the genes identified according to the invention and thereby determining the presence of a cancerous state in a sample derived from a patient to be tested, of the predisposition to develop cancer at a subsequent time in said patient.

[0081] In employing the methods of the invention, it should be borne in mind that gene or marker expression indicative of a cancerous state need not be characteristic of every cell found to be cancerous. Thus, the methods disclosed herein are useful for detecting the presence of a cancerous condition within a tissue where less than all cells exhibit the complete pattern of over-expression. For example, a set of selected genes or markers, comprising sequences homologous under stringent conditions, or at least 90%, preferably 95%, identical to at least one of the sequences as identified in FIG. **2-6**, **9-13**, **16** or **17**, may be found, using appropriate probes, either DNA or RNA, to be present in as little as 60% of cells derived from a sample of tumorous, or malignant, tissue while being absent from as much as 60% of cells derived from corresponding non-cancerous, or otherwise normal, tissue (and thus being present in as much as 40% of such normal tissue cells). In one embodiment, such expression pattern is found to be present in at least 70% of cells drawn from a cancerous tissue and absent from at least 70% of a corresponding normal, non-cancerous, tissue sample. In another embodiment, such expression pattern is found to be present in at least 80% of cells drawn from a cancerous tissue and absent from at least 80% of a corresponding normal, non-cancerous, tissue sample. In another embodiment, such expression pattern is found to be present in at least 90% of cells drawn from a cancerous tissue and absent from at least 90% of a corresponding normal, non-cancerous, tissue sample. In another embodiment, such expression pattern is found to be present in at least 100% of cells drawn from a cancerous tissue and absent from at least 100% of a corresponding normal, non-cancerous, tissue sample, although the latter embodiment may represent a rare occurrence.

[0082] In some embodiments molecular profiling includes detection, analysis, or quantification of nucleic acid (DNA, or RNA), protein, or a combination thereof. The diseases or conditions to be diagnosed by the methods of the present invention include for example conditions of abnormal growth in one or more tissues of a subject including but not limited to skin, heart, lung, kidney, breast, pancreas, liver, muscle, smooth muscle, bladder, gall bladder, colon, intestine, brain, esophagus, or prostate. In some embodiments, the tissues analyzed by the methods of the present invention include thyroid tissues.

[0083] In some embodiments, the diseases or conditions diagnosed by the methods of the present invention include benign and malignant hyperproliferative disorders including but not limited to cancers, hyperplasias, or neoplasias. In some cases, the hyperproliferative disorders diagnosed by the methods of the present invention include but are not limited to breast cancer such as a ductal carcinoma in duct tissue in a mammary gland, medullary carcinomas, colloid carcinomas, tubular carcinomas, and inflammatory breast cancer; ovarian cancer, including epithelial ovarian tumors such as adenocarcinoma in the ovary and an adenocarcinoma that has migrated from the ovary into the abdominal cavity; uterine cancer; cervical cancer such as adenocarcinoma in the cervix epithelial including squamous cell carcinoma and adenocarcinomas; prostate cancer, such as a prostate cancer selected from the following: an adenocarcinoma or an adenocarinoma that has migrated to the bone; pancreatic cancer such as epitheliod carcinoma in the pancreatic duct tissue and an adenocarcinoma in a pancreatic duct; bladder cancer such as a transitional cell carcinoma in urinary bladder, urothelial carcinomas (transitional cell carcinomas), tumors in the urothelial cells that line the bladder, squamous cell carcinomas, adenocarcinomas, and small cell cancers; leukemia such as acute myeloid leukemia (AML), acute lymphocytic leukemia, chronic lymphocytic leukemia, chronic myeloid leukemia, hairy cell leukemia, myelodysplasia, myeloproliferative disorders, acute myelogenous leukemia (AML), chronic myelogenous leukemia (CML), mastocytosis, chronic lymphocytic leukemia (CLL), multiple myeloma (MM), and myelodysplastic syndrome (MDS); bone cancer; lung cancer such as non-small cell lung cancer (NSCLC), which is divided into squamous cell carcinomas, adenocarcinomas, and large cell undifferentiated carcinomas, and small cell lung cancer; skin cancer such as basal cell carcinoma, melanoma, squamous cell carcinoma and actinic keratosis, which is a skin condition that sometimes develops into squamous cell carcinoma; eye retinoblastoma; cutaneous or intraocular (eye) melanoma; primary liver cancer (cancer that begins in the liver); kidney cancer; AIDS-related lymphoma such as diffuse large B-cell lymphoma, B-cell immunoblastic lymphoma and small non-cleaved cell lymphoma; Kaposi's Sarcoma; viral-induced cancers including hepatitis B virus (HBV), hepatitis C virus (HCV), and hepatocellular carcinoma; human lymphotropic virus-type 1 (HTLV-1) and adult T-cell leukemia/lymphoma; and human papilloma virus (HPV) and cervical cancer; central nervous system cancers (CNS) such as primary brain tumor, which includes gliomas (astrocytoma, anaplastic astrocytoma, or glioblastoma multiforme), Oligodendroglioma, Ependymoma, Meningioma, Lymphoma, Schwannoma, and Medulloblastoma; peripheral nervous system (PNS) cancers such as acoustic neuromas and malignant peripheral nerve sheath tumor (MPNST) including neurofibromas and schwannomas, malignant fibrous cytoma, malignant fibrous histiocytoma, malignant meningioma, malignant mesothelioma, and malignant mixed Müllerian tumor; oral cavity and oropharyngeal cancer such as, hypopharyngeal cancer, laryngeal cancer, nasopharyngeal cancer, and oropharyngeal cancer; stomach cancer such as lymphomas, gastric stromal tumors, and carcinoid tumors; testicular cancer such as germ cell tumors (GCTs), which include seminomas and nonseminomas, and gonadal stromal tumors, which include Leydig cell tumors and Sertoli cell tumors; thymus cancer such as to thymomas, thymic carcinomas, Hodgkin disease, non-Hodgkin lymphomas carcinoids or carcinoid tumors; rectal cancer; and colon cancer. In some cases, the diseases or conditions diagnosed by the methods of the present invention include but are not limited to thyroid disorders such as for example benign thyroid disorders including but not limited to follicular adenomas, Hurthle cell adenomas, lymphocytic throiditis, and thyroid hyperplasia. In some cases, the diseases or conditions diag-

nosed by the methods of the present invention include but are not limited to malignant thyroid disorders such as for example follicular carcinomas, follicular variant of papillary thyroid carcinomas, medullary carcinomas, and papillary carcinomas. In some cases, the methods of the present invention provide for a diagnosis of a tissue as diseased or normal. In other cases, the methods of the present invention provide for a diagnosis of normal, benign, or malignant. In some cases, the methods of the present invention provide for a diagnosis of benign/normal, or malignant. In some cases, the methods of the present invention provide for a diagnosis of one or more of the specific diseases or conditions provided herein.

II. Obtaining a Biological Sample

[0084] In some embodiments, the methods of the present invention provide for obtaining a sample from a subject. As used herein, the term subject refers to any animal (e.g. a mammal), including but not limited to humans, non-human primates, rodents, dogs, pigs, and the like. The methods of obtaining provided herein include methods of biopsy including fine needle aspiration, core needle biopsy, vacuum assisted biopsy, incisional biopsy, excisional biopsy, punch biopsy, shave biopsy or skin biopsy. The sample may be obtained from any of the tissues provided herein including but not limited to skin, heart, lung, kidney, breast, pancreas, liver, muscle, smooth muscle, bladder, gall bladder, colon, intestine, brain, prostate, esophagus, or thyroid. Alternatively, the sample may be obtained from any other source including but not limited to blood, sweat, hair follicle, buccal tissue, tears, menses, feces, or saliva. In some embodiments of the present invention, a medical professional may obtain a biological sample for testing. In some cases the medical professional may refer the subject to a testing center or laboratory for submission of the biological sample. In other cases, the subject may provide the sample. In some cases, a molecular profiling business of the present invention may obtain the sample.

[0085] The sample may be obtained by methods known in the art such as the biopsy methods provided herein, swabbing, scraping, phlebotomy, or any other methods known in the art. In some cases, the sample may be obtained, stored, or transported using components of a kit of the present invention. In some cases, multiple samples, such as multiple thyroid samples may be obtained for diagnosis by the methods of the present invention. In some cases, multiple samples, such as one or more samples from one tissue type (e.g. thyroid) and one or more samples from another tissue (e.g. buccal) may be obtained for diagnosis by the methods of the present invention. In some cases, multiple samples such as one or more samples from one tissue type (e.g. thyroid) and one or more samples from another tissue (e.g. buccal) may be obtained at the same or different times. In some cases, the samples obtained at different times are stored and/or analyzed by different methods. For example, a sample may be obtained and analyzed by cytological analysis (routine staining). In some cases, further sample may be obtained from a subject based on the results of a cytological analysis. The diagnosis of cancer may include an examination of a subject by a physician, nurse or other medical professional. The examination may be part of a routine examination, or the examination may be due to a specific complaint including but not limited to one of the following: pain, illness, anticipation of illness, presence of a suspicious lump or mass, a disease, or a condition. The subject may or may not be aware of the disease or condition. The medical professional may obtain a biological sample for testing. In some cases the medical professional may refer the subject to a testing center or laboratory for submission of the biological sample.

[0086] In some cases, the subject may be referred to a specialist such as an oncologist, surgeon, or endocrinologist for further diagnosis. The specialist may likewise obtain a biological sample for testing or refer the individual to a testing center or laboratory for submission of the biological sample. In any case, the biological sample may be obtained by a physician, nurse, or other medical professional such as a medical technician, endocrinologist, cytologist, phlebotomist, radiologist, or a pulmonologist. The medical professional may indicate the appropriate test or assay to perform on the sample, or the molecular profiling business of the present disclosure may consult on which assays or tests are most appropriately indicated. The molecular profiling business may bill the individual or medical or insurance provider thereof for consulting work, for sample acquisition and or storage, for materials, or for all products and services rendered.

[0087] In some embodiments of the present invention, a medical professional need not be involved in the initial diagnosis or sample acquisition. An individual may alternatively obtain a sample through the use of an over the counter kit. Said kit may contain a means for obtaining said sample as described herein, a means for storing said sample for inspection, and instructions for proper use of the kit. In some cases, molecular profiling services are included in the price for purchase of the kit. In other cases, the molecular profiling services are billed separately.

[0088] A sample suitable for use by the molecular profiling business may be any material containing tissues, cells, nucleic acids, genes, gene fragments, expression products, gene expression products, or gene expression product fragments of an individual to be tested. Methods for determining sample suitability and/or adequacy are provided. A sample may include but is not limited to, tissue, cells, or biological material from cells or derived from cells of an individual. The sample may be a heterogeneous or homogeneous population of cells or tissues. The biological sample may be obtained using any method known to the art that can provide a sample suitable for the analytical methods described herein.

[0089] The sample may be obtained by non-invasive methods including but not limited to: scraping of the skin or cervix, swabbing of the cheek, saliva collection, urine collection, feces collection, collection of menses, tears, or semen. In other cases, the sample is obtained by an invasive procedure including but not limited to: biopsy, alveolar or pulmonary lavage, needle aspiration, or phlebotomy. The method of biopsy may further include incisional biopsy, excisional biopsy, punch biopsy, shave biopsy, or skin biopsy. The method of needle aspiration may further include fine needle aspiration, core needle biopsy, vacuum assisted biopsy, or large core biopsy. In some embodiments, multiple samples may be obtained by the methods herein to ensure a sufficient amount of biological material. Methods of obtaining suitable samples of thyroid are known in the art and are further described in the ATA Guidelines for thyroid nodule management (Cooper et al. *Thyroid Vol.* 16 No. 2 2006), herein incorporated by reference in its entirety. Generic

methods for obtaining biological samples are also known in the art and further described in for example Ramzy, Ibrahim *Clinical Cytopathology and Aspiration Biopsy* 2001 which is herein incorporated by reference in its entirety. In one embodiment, the sample is a fine needle aspirate of a thyroid nodule or a suspected thyroid tumor. In some cases, the fine needle aspirate sampling procedure may be guided by the use of an ultrasound, X-ray, or other imaging device.

[0090] In some embodiments of the present invention, the molecular profiling business may obtain the biological sample from a subject directly, from a medical professional, from a third party, or from a kit provided by the molecular profiling business or a third party. In some cases, the biological sample may be obtained by the molecular profiling business after the subject, a medical professional, or a third party acquires and sends the biological sample to the molecular profiling business. In some cases, the molecular profiling business may provide suitable containers, and excipients for storage and transport of the biological sample to the molecular profiling business.

III. Storing the Sample

[0091] In some embodiments, the methods of the present invention provide for storing the sample for a time such as seconds, minutes, hours, days, weeks, months, years or longer after the sample is obtained and before the sample is analyzed by one or more methods of the invention. In some cases, the sample obtained from a subject is subdivided prior to the step of storage or further analysis such that different portions of the sample are subject to different downstream methods or processes including but not limited to storage, cytological analysis, adequacy tests, nucleic acid extraction, molecular profiling or a combination thereof.

[0092] In some cases, a portion of the sample may be stored while another portion of said sample is further manipulated. Such manipulations may include but are not limited to molecular profiling; cytological staining; nucleic acid (RNA or DNA) extraction, detection, or quantification; gene expression product (RNA or Protein) extraction, detection, or quantification; fixation; and examination. The sample may be fixed prior to or during storage by any method known to the art such as using glutaraldehyde, formaldehyde, or methanol. In other cases, the sample is obtained and stored and subdivided after the step of storage for further analysis such that different portions of the sample are subject to different downstream methods or processes including but not limited to storage, cytological analysis, adequacy tests, nucleic acid extraction, molecular profiling or a combination thereof. In some cases, samples are obtained and analyzed by for example cytological analysis, and the resulting sample material is further analyzed by one or more molecular profiling methods of the present invention. In such cases, the samples may be stored between the steps of cytological analysis and the steps of molecular profiling. Samples may be stored upon acquisition to facilitate transport, or to wait for the results of other analyses. In another embodiment, samples may be stored while awaiting instructions from a physician or other medical professional.

[0093] The acquired sample may be placed in a suitable medium, excipient, solution, or container for short term or long term storage. Said storage may require keeping the sample in a refrigerated, or frozen environment. The sample may be quickly frozen prior to storage in a frozen environment. The frozen sample may be contacted with a suitable cryopreservation medium or compound including but not limited to: glycerol, ethylene glycol, sucrose, or glucose. A suitable medium, excipient, or solution may include but is not limited to: hanks salt solution, saline, cellular growth medium, an ammonium salt solution such as ammonium sulphate or ammonium phosphate, or water. Suitable concentrations of ammonium salts include solutions of about 0.1 g/ml, 0.2 g/ml, 0.3 g/ml, 0.4 g/ml, 0.5 g/ml, 0.6 g/ml, 0.7 g/ml, 0.8 g/ml, 0.9 g/ml, 1.0 g/ml, 1.1 g/ml, 1.2 g/ml, 1.3 g/ml, 1.4 g/ml, 1.5 g/ml, 1.6 g/ml, 1.7 g/ml, 1.8 g/ml, 1.9 g/ml, 2.0 g/ml, 2.2 g/ml, 2.3 g/ml, 2.5 g/ml or higher. The medium, excipient, or solution may or may not be sterile.

[0094] The sample may be stored at room temperature or at reduced temperatures such as cold temperatures (e.g. between about 20° C. and about 0° C.), or freezing temperatures, including for example 0 C, −1 C, −2 C, −3 C, −4 C, −5 C, −6 C, −7 C, −8 C, −9 C, −10 C, −12 C, −14 C, −15 C, −16 C, −20 C, −22 C, −25 C, −28 C, −30 C, −35 C, −40 C, −45 C, −50 C, −60 C, −70 C, −80 C, −100 C, −120 C, −140 C, −180 C, −190 C, or about −200 C. In some cases, the samples may be stored in a refrigerator, on ice or a frozen gel pack, in a freezer, in a cryogenic freezer, on dry ice, in liquid nitrogen, or in a vapor phase equilibrated with liquid nitrogen.

[0095] The medium, excipient, or solution may contain preservative agents to maintain the sample in an adequate state for subsequent diagnostics or manipulation, or to prevent coagulation. Said preservatives may include citrate, ethylene diamine tetraacetic acid, sodium azide, or thimersol. The medium, excipient or solution may contain suitable buffers or salts such as Tris buffers or phosphate buffers, sodium salts (e.g. NaCl), calcium salts, magnesium salts, and the like. In some cases, the sample may be stored in a commercial preparation suitable for storage of cells for subsequent cytological analysis such as but not limited to Cytyc ThinPrep, SurePath, or Monoprep.

[0096] The sample container may be any container suitable for storage and or transport of the biological sample including but not limited to: a cup, a cup with a lid, a tube, a sterile tube, a vacuum tube, a syringe, a bottle, a microscope slide, or any other suitable container. The container may or may not be sterile.

IV. Transportation of the Sample

[0097] The methods of the present invention provide for transport of the sample. In some cases, the sample is transported from a clinic, hospital, doctor's office, or other location to a second location whereupon the sample may be stored and/or analyzed by for example, cytological analysis or molecular profiling. In some cases, the sample may be transported to a molecular profiling company in order to perform the analyses described herein. In other cases, the sample may be transported to a laboratory such as a laboratory authorized or otherwise capable of performing the methods of the present invention such as a Clinical Laboratory Improvement Amendments (CLIA) laboratory. The sample may be transported by the individual from whom the sample derives. Said transportation by the individual may include the individual appearing at a molecular profiling business or a designated sample receiving point and providing a sample. Said providing of the sample may involve any of the techniques of sample acquisition described herein, or the sample may have already have been acquired and stored in a suitable container as described herein. In other cases the

sample may be transported to a molecular profiling business using a courier service, the postal service, a shipping service, or any method capable of transporting the sample in a suitable manner. In some cases, the sample may be provided to a molecular profiling business by a third party testing laboratory (e.g. a cytology lab). In other cases, the sample may be provided to a molecular profiling business by the subject's primary care physician, endocrinologist or other medical professional. The cost of transport may be billed to the individual, medical provider, or insurance provider. The molecular profiling business may begin analysis of the sample immediately upon receipt, or may store the sample in any manner described herein. The method of storage may or may not be the same as chosen prior to receipt of the sample by the molecular profiling business.

[0098] The sample may be transported in any medium or excipient including any medium or excipient provided herein suitable for storing the sample such as a cryopreservation medium or a liquid based cytology preparation. In some cases, the sample may be transported frozen or refrigerated such as at any of the suitable sample storage temperatures provided herein.

[0099] Upon receipt of the sample by the molecular profiling business, a representative or licensee thereof, a medical professional, researcher, or a third party laboratory or testing center (e.g. a cytology laboratory) the sample may be assayed using a variety of routine analyses known to the art such as cytological assays, and genomic analysis. Such tests may be indicative of cancer, the type of cancer, any other disease or condition, the presence of disease markers, or the absence of cancer, diseases, conditions, or disease markers. The tests may take the form of cytological examination including microscopic examination as described below. The tests may involve the use of one or more cytological stains. The biological material may be manipulated or prepared for the test prior to administration of the test by any suitable method known to the art for biological sample preparation. The specific assay performed may be determined by the molecular profiling company, the physician who ordered the test, or a third party such as a consulting medical professional, cytology laboratory, the subject from whom the sample derives, or an insurance provider. The specific assay may be chosen based on the likelihood of obtaining a definite diagnosis, the cost of the assay, the speed of the assay, or the suitability of the assay to the type of material provided.

V. Test for Adequacy

[0100] Subsequent to or during sample acquisition, including before or after a step of storing the sample, the biological material may be collected and assessed for adequacy, for example, to assess the suitability of the sample for use in the methods and compositions of the present invention. The assessment may be performed by the individual who obtains the sample, the molecular profiling business, the individual using a kit, or a third party such as a cytological lab, pathologist, endocrinologist, or a researcher. The sample may be determined to be adequate or inadequate for further analysis due to many factors including but not limited to: insufficient cells, insufficient genetic material, insufficient protein, DNA, or RNA, inappropriate cells for the indicated test, or inappropriate material for the indicated test, age of the sample, manner in which the sample was obtained, or manner in which the sample was stored or transported. Adequacy may be determined using a variety of methods known in the art such as a cell staining procedure, measurement of the number of cells or amount of tissue, measurement of total protein, measurement of nucleic acid, visual examination, microscopic examination, or temperature or pH determination. In one embodiment, sample adequacy will be determined from the results of performing a gene expression product level analysis experiment. In another embodiment sample adequacy will be determined by measuring the content of a marker of sample adequacy. Such markers include elements such as iodine, calcium, magnesium, phosphorous, carbon, nitrogen, sulfur, iron etc.; proteins such as but not limited to thyroglobulin; cellular mass; and cellular components such as protein, nucleic acid, lipid, or carbohydrate.

[0101] In some cases, iodine may be measured by a chemical method such as described in U.S. Pat. No. 3,645,691 which is incorporated herein by reference in its entirety or other chemical methods known in the art for measuring iodine content. Chemical methods for iodine measurement include but are not limited to methods based on the Sandell and Kolthoff reaction. Said reaction proceeds according to the following equation:

$$2Ce^{4+}+As^{3}+\rightarrow 2Ce^{3+}+As^{5}+I.$$

[0102] Iodine has a catalytic effect upon the course of the reaction, i.e., the more iodine present in the preparation to be analyzed, the more rapidly the reaction proceeds. The speed of reaction is proportional to the iodine concentration. In some cases, this analytical method may carried out in the following manner:

[0103] A predetermined amount of a solution of arsenous oxide As_2O_3 in concentrated sulfuric or nitric acid is added to the biological sample and the temperature of the mixture is adjusted to reaction temperature, i.e., usually to a temperature between 20° C. and 60° C. A predetermined amount of a cerium (IV) sulfate solution in sulfuric or nitric acid is added thereto. Thereupon, the mixture is allowed to react at the predetermined temperature for a definite period of time. Said reaction time is selected in accordance with the order of magnitude of the amount of iodine to be determined and with the respective selected reaction temperature. The reaction time is usually between about 1 minute and about 40 minutes. Thereafter, the content of the test solution of cerium (IV) ions is determined photometrically. The lower the photometrically determined cerium (IV) ion concentration is, the higher is the speed of reaction and, consequently, the amount of catalytic agent, i.e., of iodine. In this manner the iodine of the sample can directly and quantitatively be determined.

[0104] In other cases, iodine content of a sample of thyroid tissue may be measured by detecting a specific isotope of iodine such as for example ^{123}I, ^{124}I, ^{125}I, and ^{131}I. In still other cases, the marker may be another radioisotope such as an isotope of carbon, nitrogen, sulfur, oxygen, iron, phosphorous, or hydrogen. The radioisotope in some instances may be administered prior to sample collection. Methods of radioisotope administration suitable for adequacy testing are well known in the art and include injection into a vein or artery, or by ingestion. A suitable period of time between administration of the isotope and acquisition of thyroid nodule sample so as to effect absorption of a portion of the isotope into the thyroid tissue may include any period of time between about a minute and a few days or about one

week including about 1 minute, 2 minutes, 5 minutes, 10 minutes, 15 minutes, ½ an hour, an hour, 8 hours, 12 hours, 24 hours, 48 hours, 72 hours, or about one, one and a half, or two weeks, and may readily be determined by one skilled in the art. Alternatively, samples may be measured for natural levels of isotopes such as radioisotopes of iodine, calcium, magnesium, carbon, nitrogen, sulfur, oxygen, iron, phosphorous, or hydrogen.

[0105] (i) Cell and/or Tissue Content Adequacy Test

[0106] Methods for determining the amount of a tissue include but are not limited to weighing the sample or measuring the volume of sample. Methods for determining the amount of cells include but are not limited to counting cells which may in some cases be performed after disaggregation with for example an enzyme such as trypsin or collagenase or by physical means such as using a tissue homogenizer for example. Alternative methods for determining the amount of cells recovered include but are not limited to quantification of dyes that bind to cellular material, or measurement of the volume of cell pellet obtained following centrifugation. Methods for determining that an adequate number of a specific type of cell is present include PCR, Q-PCR, RT-PCR, immuno-histochemical analysis, cytological analysis, microscopic, and or visual analysis.

[0107] (ii) Nucleic Acid Content Adequacy Test

[0108] Samples may be analyzed by determining nucleic acid content after extraction from the biological sample using a variety of methods known to the art. In some cases, nucleic acids such as RNA or mRNA is extracted from other nucleic acids prior to nucleic acid content analysis. Nucleic acid content may be extracted, purified, and measured by ultraviolet absorbance, including but not limited to aborbance at 260 nanometers using a spectrophotometer. In other cases nucleic acid content or adequacy may be measured by fluorometer after contacting the sample with a stain. In still other cases, nucleic acid content or adequacy may be measured after electrophoresis, or using an instrument such as an agilent bioanalyzer for example. It is understood that the methods of the present invention are not limited to a specific method for measuring nucleic acid content and or integrity.

[0109] In some embodiments, the RNA quantity or yield from a given sample is measured shortly after purification using a NanoDrop spectrophotometer in a range of nano- to micrograms. In some embodiments, RNA quality is measured using an Agilent 2100 Bioanalyzer instrument, and is characterized by a calculated RNA Integrity Number (RIN, 1-10). The NanoDrop is a cuvette-free spectrophotometer. It uses 1 microleter to measure from 5 ng/μl to 3,000 ng/μl of sample. The key features of NanoDrop include low volume of sample and no cuvette; large dynamic range 5 ng/μl to 3,000 ng/μl; and it allows quantitation of DNA, RNA and proteins. NanoDrop™ 2000c allows for the analysis of 0.5 μl-2.0 μl samples, without the need for cuvettes or capillaries.

[0110] RNA quality can be measured by a calculated RNA Integrity Number (RIN). The RNA integrity number (RIN) is an algorithm for assigning integrity values to RNA measurements. The integrity of RNA is a major concern for gene expression studies and traditionally has been evaluated using the 28S to 18S rRNA ratio, a method that has been shown to be inconsistent. The RIN algorithm is applied to electrophoretic RNA measurements and based on a combination of different features that contribute information about the RNA integrity to provide a more robust universal measure. In some embodiments, RNA quality is measured using an Agilent 2100 Bioanalyzer instrument. The protocols for measuring RNA quality are known and available commercially, for example, at Agilent website. Briefly, in the first step, researchers deposit total RNA sample into an RNA Nano LabChip. In the second step, the LabChip is inserted into the Agilent bioanalyzer and let the analysis run, generating a digital electropherogram. In the third step, the new RIN algorithm then analyzes the entire electrophoretic trace of the RNA sample, including the presence or absence of degradation products, to determine sample integrity. Then, The algorithm assigns a 1 to 10 RIN score, where level 10 RNA is completely intact. Because interpretation of the electropherogram is automatic and not subject to individual interpretation, universal and unbiased comparison of samples is enabled and repeatability of experiments is improved. The RIN algorithm was developed using neural networks and adaptive learning in conjunction with a large database of eukaryote total RNA samples, which were obtained mainly from human, rat, and mouse tissues. Advantages of RIN include obtain a numerical assessment of the integrity of RNA; directly comparing RNA samples, e.g. before and after archival, compare integrity of same tissue across different labs; and ensuring repeatability of experiments, e.g. if RIN shows a given value and is suitable for microarray experiments, then the RIN of the same value can always be used for similar experiments given that the same organism/tissue/extraction method is used (Schroeder A, et al. BMC Molecular Biology 2006, 7:3 (2006)).

[0111] In some embodiments, RNA quality is measured on a scale of RIN 1 to 10, 10 being highest quality. In one aspect, the present invention provides a method of analyzing gene expression from a sample with an RNA RIN value equal or less than 6.0. In some embodiments, a sample containing RNA with an RIN number of 1.0, 2.0, 3.0, 4.0, 5.0 or 6.0 is analyzed for microarray gene expression using the subject methods and algorithms of the present invention. In some embodiments, the sample is a fine needle aspirate of thyroid tissue. The sample can be degraded with an RIN as low as 2.0.

[0112] Determination of gene expression in a given sample is a complex, dynamic, and expensive process. RNA samples with RIN ≤5.0 are typically not used for multi-gene microarray analysis, and may instead be used only for single-gene RT-PCR and/or TaqMan assays. This dichotomy in the usefulness of RNA according to quality has thus far limited the usefulness of samples and hampered research efforts. The present invention provides methods via which low quality RNA can be used to obtain meaningful multi-gene expression results from samples containing low concentrations of RNA, for example, thyroid FNA samples.

[0113] In addition, samples having a low and/or un-measurable RNA concentration by NanoDrop normally deemed inadequate for multi-gene expression profiling can be measured and analyzed using the subject methods and algorithms of the present invention. The most sensitive and "state of the art" apparatus used to measure nucleic acid yield in the laboratory today is the NanoDrop spectrophotometer. Like many quantitative instruments of its kind, the accuracy of a NanoDrop measurement decreases significantly with very low RNA concentration. The minimum amount of RNA necessary for input into a microarray experiment also limits the usefulness of a given sample. In the present invention, a sample containing a very low

amount of nucleic acid can be estimated using a combination of the measurements from both the NanoDrop and the Bioanalyzer instruments, thereby optimizing the sample for multi-gene expression assays and analysis.

[0114] (iii) Protein Content Adequacy Test

[0115] In some cases, protein content in the biological sample may be measured using a variety of methods known to the art, including but not limited to: ultraviolet absorbance at 280 nanometers, cell staining as described herein, or protein staining with for example coomassie blue, or bichichonic acid. In some cases, protein is extracted from the biological sample prior to measurement of the sample. In some cases, multiple tests for adequacy of the sample may be performed in parallel, or one at a time. In some cases, the sample may be divided into aliquots for the purpose of performing multiple diagnostic tests prior to, during, or after assessing adequacy. In some cases, the adequacy test is performed on a small amount of the sample which may or may not be suitable for further diagnostic testing. In other cases, the entire sample is assessed for adequacy. In any case, the test for adequacy may be billed to the subject, medical provider, insurance provider, or government entity.

[0116] In some embodiments of the present invention, the sample may be tested for adequacy soon or immediately after collection. In some cases, when the sample adequacy test does not indicate a sufficient amount sample or sample of sufficient quality, additional samples may be taken.

VI. Analysis of Sample

[0117] In one aspect, the present invention provides methods for performing microarray gene expression analysis with low quantity and quality of polynucleotide, such as DNA or RNA. In some embodiments, the present disclosure describes methods of diagnosing, characterizing and/or monitoring a cancer by analyzing gene expression with low quantity and quality of RNA. In one embodiment, the cancer is thyroid cancer. Thyroid RNA can be obtained from fine needle aspirates (FNA). In some embodiments, gene expression profile is obtained from degraded samples with an RNA RIN value of 9.0, 8.0, 7.0, 6.0, 5.0, 4.0, 3.0, 2.0, 1.0 or less. In particular embodiments, gene expression profile is obtained from a sample with an RIN of equal or less than 6, i.e. 6.0, 5.0, 4.0, 3.0, 2.0, 1.0 or less. Provided by the present invention are methods by which low quality RNA can be used to obtain meaningful gene expression results from samples containing low concentrations of nucleic acid, such as thyroid FNA samples.

[0118] Another estimate of sample usefulness is RNA yield, typically measured in nanogram to microgram amounts for gene expression assays. The most sensitive and "state of the art" apparatus used to measure nucleic acid yield in the laboratory today is the NanoDrop spectrophotometer. Like many quantitative instruments of its kind, the accuracy of a NanoDrop measurement decreases significantly with very low RNA concentration. The minimum amount of RNA necessary for input into a microarray experiment also limits the usefulness of a given sample. In some aspects, the present invention solves the low RNA concentration problem by estimating sample input using a combination of the measurements from both the NanoDrop and the Bioanalyzer instruments. Since the quality of data obtained from a gene expression study is dependent on RNA quantity, meaningful gene expression data can be generated from samples having a low or un-measurable RNA concentration as measured by NanoDrop.

[0119] The subject methods and algorithms enable: 1) gene expression analysis of samples containing low amount and/or low quality of nucleic acid; 2) a significant reduction of false positives and false negatives, 3) a determination of the underlying genetic, metabolic, or signaling pathways responsible for the resulting pathology, 4) the ability to assign a statistical probability to the accuracy of the diagnosis of genetic disorders, 5) the ability to resolve ambiguous results, and 6) the ability to distinguish between subtypes of cancer.

[0120] Cytological Analysis

[0121] Samples may be analyzed by cell staining combined with microscopic examination of the cells in the biological sample. Cell staining, or cytological examination, may be performed by a number of methods and suitable reagents known to the art including but not limited to: EA stains, hematoxylin stains, cytostain, papanicolaou stain, eosin, nissl stain, toluidine blue, silver stain, azocarmine stain, neutral red, or janus green. In some cases the cells are fixed and/or permeablized with for example methanol, ethanol, glutaraldehyde or formaldehyde prior to or during the staining procedure. In some cases, the cells are not fixed. In some cases, more than one stain is used in combination. In other cases no stain is used at all. In some cases measurement of nucleic acid content is performed using a staining procedure, for example with ethidium bromide, hematoxylin, nissl stain or any nucleic acid stain known to the art.

[0122] In some embodiments of the present invention, cells may be smeared onto a slide by standard methods well known in the art for cytological examination. In other cases, liquid based cytology (LBC) methods may be utilized. In some cases, LBC methods provide for an improved means of cytology slide preparation, more homogenous samples, increased sensitivity and specificity, and improved efficiency of handling of samples. In liquid based cytology methods, biological samples are transferred from the subject to a container or vial containing a liquid cytology preparation solution such as for example Cytyc ThinPrep, SurePath, or Monoprep or any other liquid based cytology preparation solution known in the art. Additionally, the sample may be rinsed from the collection device with liquid cytology preparation solution into the container or vial to ensure substantially quantitative transfer of the sample. The solution containing the biological sample in liquid based cytology preparation solution may then be stored and/or processed by a machine or by one skilled in the art to produce a layer of cells on a glass slide. The sample may further be stained and examined under the microscope in the same way as a conventional cytological preparation.

[0123] In some embodiments of the present invention, samples may be analyzed by immuno-histochemical staining. Immuno-histochemical staining provides for the analysis of the presence, location, and distribution of specific molecules or antigens by use of antibodies in a biological sample (e.g. cells or tissues). Antigens may be small molecules, proteins, peptides, nucleic acids or any other molecule capable of being specifically recognized by an antibody. Samples may be analyzed by immuno-histochemical methods with or without a prior fixing and/or permeabilization step. In some cases, the antigen of interest may be detected by contacting the sample with an antibody specific for the antigen and then non-specific binding may be

removed by one or more washes. The specifically bound antibodies may then be detected by an antibody detection reagent such as for example a labeled secondary antibody, or a labeled avidin/streptavidin. In some cases, the antigen specific antibody may be labeled directly instead. Suitable labels for immuno-histochemistry include but are not limited to fluorophores such as fluoroscein and rhodamine, enzymes such as alkaline phosphatase and horse radish peroxidase, and radionuclides such as ^{32}P and ^{125}I. Gene product markers that may be detected by immuno-histochemical staining include but are not limited to Her2/Neu, Ras, Rho, EGFR, VEGFR, UbcH10, RET/PTC1, cytokeratin 20, calcitonin, GAL-3, thyroid peroxidase, and thyroglobulin.

VII. Assay Results

[0124] The results of routine cytological or other assays may indicate a sample as negative (cancer, disease or condition free), ambiguous or suspicious (suggestive of the presence of a cancer, disease or condition), diagnostic (positive diagnosis for a cancer, disease or condition), or non diagnostic (providing inadequate information concerning the presence or absence of cancer, disease, or condition). The diagnostic results may be further classified as malignant or benign. The diagnostic results may also provide a score indicating for example, the severity or grade of a cancer, or the likelihood of an accurate diagnosis, such as via a p-value, a corrected p-value, or a statistical confidence indicator. In some cases, the diagnostic results may be indicative of a particular type of a cancer, disease, or condition, such as for example follicular adenoma, Hurthle cell adenoma, lymphocytic thyroiditis, hyperplasia, follicular carcinoma, follicular variant of papillary thyroid carcinoma, papillary carcinoma, or any of the diseases or conditions provided herein. In some cases, the diagnostic results may be indicative of a particular stage of a cancer, disease, or condition. The diagnostic results may inform a particular treatment or therapeutic intervention for the type or stage of the specific cancer disease or condition diagnosed. In some embodiments, the results of the assays performed may be entered into a database. The molecular profiling company may bill the individual, insurance provider, medical provider, or government entity for one or more of the following: assays performed, consulting services, reporting of results, database access, or data analysis. In some cases all or some steps other than molecular profiling are performed by a cytological laboratory or a medical professional.

VIII. Molecular Profiling

[0125] Cytological assays mark the current diagnostic standard for many types of suspected tumors including for example thyroid tumors or nodules. In some embodiments of the present invention, samples that assay as negative, indeterminate, diagnostic, or non diagnostic may be subjected to subsequent assays to obtain more information. In the present invention, these subsequent assays comprise the steps of molecular profiling of genomic DNA, RNA, mRNA expression product levels, miRNA levels, gene expression product levels or gene expression product alternative splicing. In some embodiments of the present invention, molecular profiling means the determination of the number (e.g. copy number) and/or type of genomic DNA in a biological sample. In some cases, the number and/or type may further be compared to a control sample or a sample considered normal. In some embodiment, genomic DNA can be analyzed for copy number variation, such as an increase (amplification) or decrease in copy number, or variants, such as insertions, deletions, truncations and the like. Molecular profiling may be performed on the same sample, a portion of the same sample, or a new sample may be acquired using any of the methods described herein. The molecular profiling company may request additional sample by directly contacting the individual or through an intermediary such as a physician, third party testing center or laboratory, or a medical professional. In some cases, samples are assayed using methods and compositions of the molecular profiling business in combination with some or all cytological staining or other diagnostic methods. In other cases, samples are directly assayed using the methods and compositions of the molecular profiling business without the previous use of routine cytological staining or other diagnostic methods. In some cases the results of molecular profiling alone or in combination with cytology or other assays may enable those skilled in the art to diagnose or suggest treatment for the subject. In some cases, molecular profiling may be used alone or in combination with cytology to monitor tumors or suspected tumors over time for malignant changes.

[0126] The molecular profiling methods of the present invention provide for extracting and analyzing protein or nucleic acid (RNA or DNA) from one or more biological samples from a subject. In some cases, nucleic acid is extracted from the entire sample obtained. In other cases, nucleic acid is extracted from a portion of the sample obtained. In some cases, the portion of the sample not subjected to nucleic acid extraction may be analyzed by cytological examination or immuno-histochemistry. Methods for RNA or DNA extraction from biological samples are well known in the art and include for example the use of a commercial kit, such as the Qiagen DNeasy Blood and Tissue Kit, or the Qiagen EZ1 RNA Universal Tissue Kit.

[0127] (i) Tissue-Type Fingerprinting

[0128] In many cases, biological samples such as those provided by the methods of the present invention of may contain several cell types or tissues, including but not limited to thyroid follicular cells, thyroid medullary cells, blood cells (RBCs, WBCs, platelets), smooth muscle cells, ducts, duct cells, basement membrane, lumen, lobules, fatty tissue, skin cells, epithelial cells, and infiltrating macrophages and lymphocytes. In the case of thyroid samples, diagnostic classification of the biological samples may involve for example primarily follicular cells (for cancers derived from the follicular cell such as papillary carcinoma, follicular carcinoma, and anaplastic thyroid carcinoma) and medullary cells (for medullary cancer). The diagnosis of indeterminate biological samples from thyroid biopsies in some cases concerns the distinction of follicular adenoma vs. follicular carcinoma. The molecular profiling signal of a follicular cell for example may thus be diluted out and possibly confounded by other cell types present in the sample. Similarly diagnosis of biological samples from other tissues or organs often involves diagnosing one or more cell types among the many that may be present in the sample.

[0129] In some embodiments, the methods of the present invention provide for an upfront method of determining the cellular make-up of a particular biological sample so that the resulting molecular profiling signatures can be calibrated against the dilution effect due to the presence of other cell

and/or tissue types. In one aspect, this upfront method is an algorithm that uses a combination of known cell and/or tissue specific gene expression patterns as an upfront mini-classifier for each component of the sample. This algorithm utilizes this molecular fingerprint to pre-classify the samples according to their composition and then apply a correction/normalization factor. This data may in some cases then feed in to a final classification algorithm which would incorporate that information to aid in the final diagnosis.

[0130] (ii) Genomic Analysis

[0131] In some embodiments, genomic sequence analysis, or genotyping, may be performed on the sample. This genotyping may take the form of mutational analysis such as single nucleotide polymorphism (SNP) analysis, insertion deletion polymorphism (InDel) analysis, variable number of tandem repeat (VNTR) analysis, copy number variation (CNV) analysis or partial or whole genome sequencing. Methods for performing genomic analyses are known to the art and may include high throughput sequencing such as but not limited to those methods described in U.S. Pat. Nos. 7,335,762; 7,323,305; 7,264,929; 7,244,559; 7,211,390; 7,361,488; 7,300,788; and 7,280,922. Methods for performing genomic analyses may also include microarray methods as described hereinafter. In some cases, genomic analysis may be performed in combination with any of the other methods herein. For example, a sample may be obtained, tested for adequacy, and divided into aliquots. One or more aliquots may then be used for cytological analysis of the present invention, one or more may be used for RNA expression profiling methods of the present invention, and one or more can be used for genomic analysis. It is further understood the present invention anticipates that one skilled in the art may wish to perform other analyses on the biological sample that are not explicitly provided herein.

[0132] (iii) Expression Product Profiling

[0133] Gene expression profiling is the measurement of the activity (the expression) of thousands of genes at once, to create a global picture of cellular function. These profiles can, for example, distinguish between cells that are actively dividing, or show how the cells react to a particular treatment. Many experiments of this sort measure an entire genome simultaneously, that is, every gene present in a particular cell. Microarray technology measures the relative activity of previously identified target genes. Sequence based techniques, like serial analysis of gene expression (SAGE, SuperSAGE) are also used for gene expression profiling. SuperSAGE is especially accurate and can measure any active gene, not just a predefined set. In an RNA, mRNA or gene expression profiling microarray, the expression levels of thousands of genes are simultaneously monitored to study the effects of certain treatments, diseases, and developmental stages on gene expression. For example, microarray-based gene expression profiling can be used to characterize gene signatures of a genetic disorder disclosed herein, or different cancer types, subtypes of a cancer, and/or cancer stages.

[0134] Expression profiling experiments often involve measuring the relative amount of gene expression products, such as mRNA, expressed in two or more experimental conditions. This is because altered levels of a specific sequence of a gene expression product suggest a changed need for the protein coded for by the gene expression product, perhaps indicating a homeostatic response or a pathological condition. For example, if breast cancer cells express higher levels of mRNA associated with a particular transmembrane receptor than normal cells do, it might be that this receptor plays a role in breast cancer. One aspect of the present invention encompasses gene expression profiling as part of an important diagnostic test for genetic disorders and cancers, particularly, thyroid cancer.

[0135] In some embodiments, RNA samples with RIN $\leq$5.0 are typically not used for multi-gene microarray analysis, and may instead be used only for single-gene RT-PCR and/or TaqMan assays. Microarray, RT-PCR and TaqMan assays are standard molecular techniques well known in the relevant art. TaqMan probe-based assays are widely used in real-time PCR including gene expression assays, DNA quantification and SNP genotyping.

[0136] In one embodiment, gene expression products related to cancer that are known to the art are profiled. Such gene expression products have been described and include but are not limited to the gene expression products detailed in U.S. Pat. Nos. 7,358,061; 7,319,011; 5,965,360; 6,436,642; and US patent applications 2003/0186248, 2005/0042222, 2003/0190602, 2005/0048533, 2005/0266443, 2006/0035244, 2006/083744, 2006/0088851, 2006/0105360, 2006/0127907, 2007/0020657, 2007/0037186, 2007/0065833, 2007/0161004, 2007/0238119, and 2008/0044824.

[0137] It is further anticipated that other gene expression products related to cancer may become known, and that the methods and compositions described herein may include such newly discovered gene expression products.

[0138] In some embodiments of the present invention gene expression products are analyzed alternatively or additionally for characteristics other than expression level. For example, gene products may be analyzed for alternative splicing. Alternative splicing, also referred to as alternative exon usage, is the RNA splicing variation mechanism wherein the exons of a primary gene transcript, the pre-mRNA, are separated and reconnected (i.e. spliced) so as to produce alternative mRNA molecules from the same gene. In some cases, these linear combinations then undergo the process of translation where a specific and unique sequence of amino acids is specified by each of the alternative mRNA molecules from the same gene resulting in protein isoforms. Alternative splicing may include incorporating different exons or different sets of exons, retaining certain introns, or using utilizing alternate splice donor and acceptor sites.

[0139] In some cases, markers or sets of markers may be identified that exhibit alternative splicing that is diagnostic for benign, malignant or normal samples. Additionally, alternative splicing markers may further provide a diagnosis for the specific type of thyroid cancer (e.g. papillary, follicular, medullary, or anaplastic). Alternative splicing markers diagnostic for malignancy known to the art include those listed in U.S. Pat. No. 6,436,642.

[0140] In some cases expression of RNA expression products that do not encode for proteins such as miRNAs, and siRNAs may be assayed by the methods of the present invention. Differential expression of these RNA expression products may be indicative of benign, malignant or normal samples. Differential expression of these RNA expression products may further be indicative of the subtype of the benign sample (e.g. FA, NHP, LCT, BN, CN, HA) or malignant sample (e.g. FC, PTC, FVPTC, ATC, MTC). In some cases, differential expression of miRNAs, siRNAs,

alternative splice RNA isoforms, mRNAs or any combination thereof may be assayed by the methods of the present invention.

[0141] In some embodiments, the current invention provides 16 panels of biomarkers, each panel being required to characterize, rule out, and diagnose pathology within the thyroid. The sixteen panels are:

[0142] 1 Normal Thyroid (NML)

[0143] 2 Lymphocytic, Autoimmune Thyroiditis (LCT)

[0144] 3 Nodular Hyperplasia (NHP)

[0145] 4 Follicular Thyroid Adenoma (FA)

[0146] 5 Hurthle Cell Thyroid Adenoma (HC)

[0147] 6 Parathyroid (non thyroid tissue)

[0148] 7 Anaplastic Thyroid Carcinoma (ATC)

[0149] 8 Follicular Thyroid Carcinoma (FC)

[0150] 9 Hurthle Cell Thyroid Carcinoma (HC)

[0151] 10 Papillary Thyroid Carcinoma (PTC)

[0152] 11 Follicular Variant of Papillary Carcinoma (FVPTC)

[0153] 12 Medullary Thyroid Carcinoma (MTC)

[0154] 13 Renal Carcinoma metastasis to the Thyroid

[0155] 14 Melanoma metastasis to the Thyroid

[0156] 15 B cell Lymphoma metastasis to the Thyroid

[0157] 16 Breast Carcinoma metastasis to the Thyroid

[0158] Each panel includes a set of biomarkers required to characterize, rule out, and diagnose a given pathology within the thyroid. Panels 1-6 describe benign pathology. Panels 7-16 describe malignant pathology.

[0159] The biological nature of the thyroid and each pathology found within it, suggests that there is redundancy between the plurality of biomarkers in one panel versus the plurality of biomarkers in another panel. Mirroring each pathology subtype, each diagnostic panel is heterogeneous and semi-redundant with the biomarkers in another panel. Heterogeneity and redundancy reflect the biology of the tissues sampled in a given FNA and the differences in gene expression that characterize each pathology subtype from one another.

[0160] In one aspect, the diagnostic value of the present invention lies in the comparison of i) one or more markers in one panel, versus ii) one or more markers in each additional panel. The utility of the invention is its higher diagnostic accuracy in FNA than presently possible by any other means.

[0161] In some embodiments, the biomarkers within each panel are interchangeable (modular). The plurality of biomarkers in all panels can be substituted, increased, reduced, or improved to accommodate the definition of new pathologic subtypes (e.g. new case reports of metastasis to the thyroid from other organs). The current invention describes the plurality of markers that define each of sixteen heterogeneous, semi-redundant, and distinct pathologies found in the thyroid. All sixteen panels are required to arrive at an accurate diagnosis, and any given panel alone does not have sufficient power to make a true diagnostic determination. In some embodiments, the biomarkers in each panel are interchanged with a suitable combination of biomarkers, such that the plurality of biomarkers in each panel still defines a given pathology subtype within the context of examining the plurality of biomarkers that define all other pathology subtypes.

[0162] Methods and compositions of the invention can have genes selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or 16 or more biomarker panels and can have from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50 or more gene expression products from each biomarker panel, in any combination. In some embodiments, the set of genes combined give a specificity or sensitivity of greater than 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 99.5%, or a positive predictive value or negative predictive value of at least 95%, 95.5%, 96%, 96.5%, 97%, 97.5%, 98%, 98.5%, 99%, 99.5% or more.

[0163] (1) In Vitro Methods of Determining Expression Product Levels

[0164] The general methods for determining gene expression product levels are known to the art and may include but are not limited to one or more of the following: additional cytological assays, assays for specific proteins or enzyme activities, assays for specific expression products including protein or RNA or specific RNA splice variants, in situ hybridization, whole or partial genome expression analysis, microarray hybridization assays, SAGE, enzyme linked immuno-absorbance assays, mass-spectrometry, immunohistochemistry, or blotting. Gene expression product levels may be normalized to an internal standard such as total mRNA or the expression level of a particular gene including but not limited to glyceraldehyde 3 phosphate dehydrogenase, or tublin.

[0165] In some embodiments of the present invention, gene expression product markers and alternative splicing markers may be determined by microarray analysis using, for example, Affymetrix arrays, cDNA microarrays, oligonucleotide microarrays, spotted microarrays, or other microarray products from Biorad, Agilent, or Eppendorf. Microarrays provide particular advantages because they may contain a large number of genes or alternative splice variants that may be assayed in a single experiment. In some cases, the microarray device may contain the entire human genome or transcriptome or a substantial fraction thereof allowing a comprehensive evaluation of gene expression patterns, genomic sequence, or alternative splicing. Markers may be found using standard molecular biology and microarray analysis techniques as described in Sambrook *Molecular Cloning a Laboratory Manual* 2001 and Baldi, P., and Hatfield, W. G., *DNA Microarrays and Gene Expression* 2002.

[0166] Microarray analysis begins with extracting and purifying nucleic acid from a biological sample, (e.g. a biopsy or fine needle aspirate) using methods known to the art. For expression and alternative splicing analysis it may be advantageous to extract and/or purify RNA from DNA. It may further be advantageous to extract and/or purify mRNA from other forms of RNA such as tRNA and rRNA.

[0167] Purified nucleic acid may further be labeled with a fluorescent, radionuclide, or chemical label such as biotin or digoxin for example by reverse transcription, PCR, ligation, chemical reaction or other techniques. The labeling can be direct or indirect which may further require a coupling stage. The coupling stage can occur before hybridization, for example, using aminoallyl-UTP and NHS amino-reactive dyes (like cyanine dyes) or after, for example, using biotin and labelled streptavidin. The modified nucleotides (e.g. at a 1 aaUTP: 4 TTP ratio) are added enzymatically at a lower rate compared to normal nucleotides, typically resulting in 1 every 60 bases (measured with a spectrophotometer). The aaDNA may then be purified with, for example, a column or a diafiltration device. The aminoallyl group is an amine

group on a long linker attached to the nucleobase, which reacts with a reactive label (e.g. a fluorescent dye).

[0168] The labeled samples may then be mixed with a hybridization solution which may contain SDS, SSC, dextran sulfate, a blocking agent (such as COT1 DNA, salmon sperm DNA, calf thymum DNA, PolyA or PolyT), Denhardt's solution, formamine, or a combination thereof.

[0169] A hybridization probe is a fragment of DNA or RNA of variable length, which is used to detect in DNA or RNA samples the presence of nucleotide sequences (the DNA target) that are complementary to the sequence in the probe. The probe thereby hybridizes to single-stranded nucleic acid (DNA or RNA) whose base sequence allows probe-target base pairing due to complementarity between the probe and target. The labeled probe is first denatured (by heating or under alkaline conditions) into single DNA strands and then hybridized to the target DNA.

[0170] To detect hybridization of the probe to its target sequence, the probe is tagged (or labeled) with a molecular marker; commonly used markers are ^{32}P or Digoxigenin, which is non-radioactive antibody-based marker. DNA sequences or RNA transcripts that have moderate to high sequence similarity to the probe are then detected by visualizing the hybridized probe via autoradiography or other imaging techniques. Detection of sequences with moderate or high similarity depends on how stringent the hybridization conditions were applied—high stringency, such as high hybridization temperature and low salt in hybridization buffers, permits only hybridization between nucleic acid sequences that are highly similar, whereas low stringency, such as lower temperature and high salt, allows hybridization when the sequences are less similar Hybridization probes used in DNA microarrays refer to DNA covalently attached to an inert surface, such as coated glass slides or gene chips, and to which a mobile cDNA target is hybridized.

[0171] This mix may then be denatured by heat or chemical means and added to a port in a microarray. The holes may then be sealed and the microarray hybridized, for example, in a hybridization oven, where the microarray is mixed by rotation, or in a mixer. After an overnight hybridization, non specific binding may be washed off (e.g. with SDS and SSC). The microarray may then be dried and scanned in a special machine where a laser excites the dye and a detector measures its emission. The image may be overlaid with a template grid and the intensities of the features (several pixels make a feature) may be quantified.

[0172] Various kits can be used for the amplification of nucleic acid and probe generation of the subject methods. Examples of kit that can be used in the present invention include but are not limited to Nugen WT-Ovation FFPE kit, cDNA amplification kit with Nugen Exon Module and Frag/Label module. The NuGEN WT-Ovation™ FFPE System V2 is a whole transcriptome amplification system that enables conducting global gene expression analysis on the vast archives of small and degraded RNA derived from FFPE samples. The system is comprised of reagents and a protocol required for amplification of as little as 50 ng of total FFPE RNA. The protocol can be used for qPCR, sample archiving, fragmentation, and labeling. The amplified cDNA can be fragmented and labeled in less than two hours for GeneChip® 3' expression array analysis using NuGEN's FL-Ovation™ cDNA Biotin Module V2. For analysis using Affymetrix GeneChip® Exon and Gene ST arrays, the amplified cDNA can be used with the WT-Ovation Exon Module, then fragmented and labeled using the FL-Ovation™ cDNA Biotin Module V2. For analysis on Agilent arrays, the amplified cDNA can be fragmented and labeled using NuGEN's FL-Ovation™ cDNA Fluorescent Module. More information on Nugen WT-Ovation FFPE kit can be obtained at http://www.nugeninc.com/nugen/index.cfm/products/amplification-systems/wt-ovation-ffpe/.

[0173] In some embodiments, Ambion WT-expression kit can be used. Ambion WT-expression kit allows amplification of total RNA directly without a separate ribosomal RNA (rRNA) depletion step. With the Ambion® WT Expression Kit, samples as small as 50 ng of total RNA can be analyzed on Affymetrix® GeneChip® Human, Mouse, and Rat Exon and Gene 1.0 ST Arrays. In addition to the lower input RNA requirement and high concordance between the Affymetrix® method and TaqMan® real-time PCR data, the Ambion® WT Expression Kit provides a significant increase in sensitivity. For example, a greater number of probe sets detected above background can be obtained at the exon level with the Ambion® WT Expression Kit as a result of an increased signal-to-noise ratio. Ambion WT-expression kit may be used in combination with additional Affymetrix labeling kit.

[0174] In some embodiments, AmpTec Trinucleotide Nano mRNA Amplification kit (6299-A15) can be used in the subject methods. The ExpressArt® TRinucleotide mRNA amplification Nano kit is suitable for a wide range, from 1 ng to 700 ng of input total RNA. According to the amount of input total RNA and the required yields of aRNA, it can be used for 1-round (input >300 ng total RNA) or g-rounds (minimal input amount 1 ng total RNA), with aRNA yields in the range of >10 μg. AmpTec's proprietary TRinucleotide priming technology results in preferential amplification of mRNAs (independent of the universal eukaryotic 3'-poly(A)-sequence), combined with selection against rRNAs. More information on AmpTec Trinucleotide Nano mRNA Amplification kit can be obtained at http://www.amp-tec.com/products.htm. This kit can be used in combination with cDNA conversion kit and Affymetrix labeling kit.

[0175] The raw data may then be normalized, for example, by subtracting the background intensity and then dividing the intensities making either the total intensity of the features on each channel equal or the intensities of a reference gene and then the t-value for all the intensities may be calculated. More sophisticated methods, include z-ratio, loess and lowess regression and RMA (robust multichip analysis) for Affymetrix chips.

[0176] (2) In Vivo Methods of Determining Gene Expression Product Levels

[0177] It is further anticipated that the methods and compositions of the present invention may be used to determine gene expression product levels in an individual without first obtaining a sample. For example, gene expression product levels may be determined in vivo, that is in the individual. Methods for determining gene expression product levels in vivo are known to the art and include imaging techniques such as CAT, MRI; NMR; PET; and optical, fluorescence, or biophotonic imaging of protein or RNA levels using antibodies or molecular beacons. Such methods are described in US 2008/0044824, US 2008/0131892, herein incorporated by reference. Additional methods for in vivo molecular profiling are contemplated to be within the scope of the present invention.

[0178] In some embodiments of the present invention, molecular profiling includes the step of binding the sample or a portion of the sample to one or more probes of the present invention. Suitable probes bind to components of the sample, i.e. gene products, that are to be measured and include but are not limited to antibodies or antibody fragments, aptamers, nucleic acids, and oligonucleotides. The binding of the sample to the probes of the present invention represents a transformation of matter from sample to sample bound to one or more probes. The method of diagnosing cancer based on molecular profiling further comprises the steps of detecting gene expression products (i.e. mRNA or protein) and levels of the sample, comparing it to an amount in a normal control sample to determine the differential gene expression product level between the sample and the control; and classifying the test sample by inputting one or more differential gene expression product levels to a trained algorithm of the present invention; validating the sample classification using the selection and classification algorithms of the present invention; and identifying the sample as positive for a genetic disorder or a type of cancer.

[0179] (i) Comparison of Sample to Normal

[0180] The results of the molecular profiling performed on the sample provided by the individual (test sample) may be compared to a biological sample that is known or suspected to be normal. A normal sample is that which is or is expected to be free of any cancer, disease, or condition, or a sample that would test negative for any cancer disease or condition in the molecular profiling assay. The normal sample may be from a different individual from the individual being tested, or from the same individual. In some cases, the normal sample is a sample obtained from a buccal swab of an individual such as the individual being tested for example. The normal sample may be assayed at the same time, or at a different time from the test sample.

[0181] The results of an assay on the test sample may be compared to the results of the same assay on a normal sample. In some cases the results of the assay on the normal sample are from a database, or a reference. In some cases, the results of the assay on the normal sample are a known or generally accepted value by those skilled in the art. In some cases the comparison is qualitative. In other cases the comparison is quantitative. In some cases, qualitative or quantitative comparisons may involve but are not limited to one or more of the following: comparing fluorescence values, spot intensities, absorbance values, chemiluminescent signals, histograms, critical threshold values, statistical significance values, gene product expression levels, gene product expression level changes, alternative exon usage, changes in alternative exon usage, protein levels, DNA polymorphisms, coy number variations, indications of the presence or absence of one or more DNA markers or regions, or nucleic acid sequences.

[0182] (ii) Evaluation of Results

[0183] In some embodiments, the molecular profiling results are evaluated using methods known to the art for correlating gene product expression levels or alternative exon usage with specific phenotypes such as malignancy, the type of malignancy (e.g. follicular carcinoma), benignancy, or normalcy (e.g. disease or condition free). In some cases, a specified statistical confidence level may be determined in order to provide a diagnostic confidence level. For example, it may be determined that a confidence level of greater than 90% may be a useful predictor of malignancy, type of malignancy, or benignancy. In other embodiments, more or less stringent confidence levels may be chosen. For example, a confidence level of approximately 70%, 75%, 80%, 85%, 90%, 95%, 97.5%, 99%, 99.5%, or 99.9% may be chosen as a useful phenotypic predictor. The confidence level provided may in some cases be related to the quality of the sample, the quality of the data, the quality of the analysis, the specific methods used, and the number of gene expression products analyzed. The specified confidence level for providing a diagnosis may be chosen on the basis of the expected number of false positives or false negatives and/or cost. Methods for choosing parameters for achieving a specified confidence level or for identifying markers with diagnostic power include but are not limited to Receiver Operator Curve analysis (ROC), binormal ROC, principal component analysis, partial least squares analysis, singular value decomposition, least absolute shrinkage and selection operator analysis, least angle regression, and the threshold gradient directed regularization method.

[0184] (iii) Data Analysis

[0185] Raw gene expression level and alternative splicing data may in some cases be improved through the application of algorithms designed to normalize and or improve the reliability of the data. In some embodiments of the present invention the data analysis requires a computer or other device, machine or apparatus for application of the various algorithms described herein due to the large number of individual data points that are processed. A "machine learning algorithm" refers to a computational-based prediction methodology, also known to persons skilled in the art as a "classifier", employed for characterizing a gene expression profile. The signals corresponding to certain expression levels, which are obtained by, e.g., microarray-based hybridization assays, are typically subjected to the algorithm in order to classify the expression profile. Supervised learning generally involves "training" a classifier to recognize the distinctions among classes and then "testing" the accuracy of the classifier on an independent test set. For new, unknown samples the classifier can be used to predict the class in which the samples belong.

[0186] In some cases, the robust multi-array Average (RMA) method may be used to normalize the raw data. The RMA method begins by computing background-corrected intensities for each matched cell on a number of microarrays. The background corrected values are restricted to positive values as described by Irizarry et al. *Biostatistics* 2003 Apr. 4 (2): 249-64. After background correction, the base-2 logarithm of each background corrected matched-cell intensity is then obtained. The back-ground corrected, log-transformed, matched intensity on each microarray is then normalized using the quantile normalization method in which for each input array and each probe expression value, the array percentile probe value is replaced with the average of all array percentile points, this method is more completely described by Bolstad et al. *Bioinformatics* 2003. Following quantile normalization, the normalized data may then be fit to a linear model to obtain an expression measure for each probe on each microarray. Tukey's median polish algorithm (Tukey, J. W., *Exploratory Data Analysis.* 1977) may then be used to determine the log-scale expression level for the normalized probe set data.

[0187] Data may further be filtered to remove data that may be considered suspect. In some embodiments, data deriving from microarray probes that have fewer than about

4, 5, 6, 7 or 8 guanosine+cytosine nucleotides may be considered to be unreliable due to their aberrant hybridization propensity or secondary structure issues. Similarly, data deriving from microarray probes that have more than about 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, or 22 guanosine+cytosine nucleotides may be considered unreliable due to their aberrant hybridization propensity or secondary structure issues.

[0188] In some cases, unreliable probe sets may be selected for exclusion from data analysis by ranking probe-set reliability against a series of reference datasets. For example, RefSeq or Ensembl (EMBL) are considered very high quality reference datasets. Data from probe sets matching RefSeq or Ensembl sequences may in some cases be specifically included in microarray analysis experiments due to their expected high reliability. Similarly data from probe-sets matching less reliable reference datasets may be excluded from further analysis, or considered on a case by case basis for inclusion. In some cases, the Ensembl high throughput cDNA (HTC) and/or mRNA reference datasets may be used to determine the probe-set reliability separately or together. In other cases, probe-set reliability may be ranked. For example, probes and/or probe-sets that match perfectly to all reference datasets such as for example RefSeq, HTC, and mRNA, may be ranked as most reliable (1). Furthermore, probes and/or probe-sets that match two out of three reference datasets may be ranked as next most reliable (2), probes and/or probe-sets that match one out of three reference datasets may be ranked next (3) and probes and/or probe sets that match no reference datasets may be ranked last (4). Probes and or probe-sets may then be included or excluded from analysis based on their ranking. For example, one may choose to include data from category 1, 2, 3, and 4 probe-sets; category 1, 2, and 3 probe-sets; category 1 and 2 probe-sets; or category 1 probe-sets for further analysis. In another example, probe-sets may be ranked by the number of base pair mismatches to reference dataset entries. It is understood that there are many methods understood in the art for assessing the reliability of a given probe and/or probe-set for molecular profiling and the methods of the present invention encompass any of these methods and combinations thereof.

[0189] In some embodiments of the present invention, data from probe-sets may be excluded from analysis if they are not expressed or expressed at an undetectable level (not above background). A probe-set is judged to be expressed above background if for any group:

[0190] Integral from T0 to Infinity of the standard normal distribution<Significance (0.01)

Where:

T0=Sqr(GroupSize) (T−P)/Sqr(Pvar),

[0191] GroupSize=Number of CEL files in the group,

T=Average of probe scores in probe-set,

P=Average of Background probes averages of GC content, and

Pvar=Sum of Background probe variances/(Number of probes in probe-set)^2,

[0192] This allows including probe-sets in which the average of probe-sets in a group is greater than the average expression of background probes of similar GC content as the probe-set probes as the center of background for the probe-set and enables one to derive the probe-set dispersion from the background probe-set variance.

[0193] In some embodiments of the present invention, probe-sets that exhibit no, or low variance may be excluded from further analysis. Low-variance probe-sets are excluded from the analysis via a Chi-Square test. A probe-set is considered to be low-variance if its transformed variance is to the left of the 99 percent confidence interval of the Chi-Squared distribution with (N−1) degrees of freedom.

(N−1)*Probe-set Variance/(Gene Probe-set Variance) ~Chi-Sq(N−1)

where N is the number of input CEL files, (N−1) is the degrees of freedom for the Chi-Squared distribution, and the 'probe-set variance for the gene' is the average of probe-set variances across the gene.

[0194] In some embodiments of the present invention, probe-sets for a given gene or transcript cluster may be excluded from further analysis if they contain less than a minimum number of probes that pass through the previously described filter steps for GC content, reliability, variance and the like. For example in some embodiments, probe-sets for a given gene or transcript cluster may be excluded from further analysis if they contain less than about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or less than about 20 probes.

[0195] Methods of data analysis of gene expression levels or of alternative splicing may further include the use of a feature selection algorithm as provided herein. In some embodiments of the present invention, feature selection is provided by use of the LIMMA software package (Smyth, G. K. (2005). Limma: linear models for microarray data. In: *Bioinformatics and Computational Biology Solutions using R and Bioconductor*, R. Gentleman, V. Carey, S. Dudoit, R. Irizarry, W. Huber (eds.), Springer, New York, pages 397-420).

[0196] Methods of data analysis of gene expression levels and or of alternative splicing may further include the use of a pre-classifier algorithm. For example, an algorithm may use a cell-specific molecular fingerprint to pre-classify the samples according to their composition and then apply a correction/normalization factor. This data/information may then be fed in to a final classification algorithm which would incorporate that information to aid in the final diagnosis.

[0197] Methods of data analysis of gene expression levels and or of alternative splicing may further include the use of a classifier algorithm as provided herein. In some embodiments of the present invention a support vector machine (SVM) algorithm, a random forest algorithm, or a combination thereof is provided for classification of microarray data. In some embodiments, identified markers that distinguish samples (e.g. benign vs. malignant, normal vs. malignant) or distinguish subtypes (e.g. PTC vs. FVPTC) are selected based on statistical significance. In some cases, the statistical significance selection is performed after applying a Benjamini Hochberg correction for false discovery rate (FDR).

[0198] In some cases, the classifier algorithm may be supplemented with a meta-analysis approach such as that described by Fishel and Kaufman et al. 2007 *Bioinformatics* 23(13): 1599-606. In some cases, the classifier algorithm may be supplemented with a meta-analysis approach such as a repeatability analysis. In some cases, the repeatability analysis selects markers that appear in at least one predictive expression product marker set.

[0199] In some cases, the results of feature selection and classification may be ranked using a Bayesian post-analysis method. For example, microarray data may be extracted, normalized, and summarized using methods known in the art such as the methods provided herein. The data may then be subjected to a feature selection step such as any feature selection methods known in the art such as the methods provided herein including but not limited to the feature selection methods provided in LIMMA. The data may then be subjected to a classification step such as any of the classification methods known in the art such as the use of any of the algorithms or methods provided herein including but not limited to the use of SVM or random forest algorithms. The results of the classifier algorithm may then be ranked by according to a posterior probability function. For example, the posterior probability function may be derived from examining known molecular profiling results, such as published results, to derive prior probabilities from type I and type II error rates of assigning a marker to a category (e.g. benign, malignant, normal, ATC, PTC, MTC, FC, FN, FA, FVPTC CN, HA, HC, LCT, NHP etc.). These error rates may be calculated based on reported sample size for each study using an estimated fold change value (e.g. 1.1, 1.2., 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.2, 2.4, 2.5, 3, 4, 5, 6, 7, 8, 9, 10 or more). These prior probabilities may then be combined with a molecular profiling dataset of the present invention to estimate the posterior probability of differential gene expression. Finally, the posterior probability estimates may be combined with a second dataset of the present invention to formulate the final posterior probabilities of differential expression. Additional methods for deriving and applying posterior probabilities to the analysis of microarray data are known in the art and have been described for example in Smyth, G. K. 2004 *Stat. Appl. Genet. Mol. Biol.* 3: Article 3. In some cases, the posterior probabilities may be used to rank the markers provided by the classifier algorithm. In some cases, markers may be ranked according to their posterior probabilities and those that pass a chosen threshold may be chosen as markers whose differential expression is indicative of or diagnostic for samples that are for example benign, malignant, normal, ATC, PTC, MTC, FC, FN, FA, FVPTC CN, HA, HC, LCT, or NHP. Illustrative threshold values include prior probabilities of 0.7, 0.75, 0.8, 0.85, 0.9, 0.925, 0.95, 0.975, 0.98, 0.985, 0.99, 0.995 or higher.

[0200] A statistical evaluation of the results of the molecular profiling may provide a quantitative value or values indicative of one or more of the following: the likelihood of diagnostic accuracy, the likelihood of cancer, disease or condition, the likelihood of a particular cancer, disease or condition, the likelihood of the success of a particular therapeutic intervention. Thus a physician, who is not likely to be trained in genetics or molecular biology, need not understand the raw data. Rather, the data is presented directly to the physician in its most useful form to guide patient care. The results of the molecular profiling can be statistically evaluated using a number of methods known to the art including, but not limited to: the students T test, the two sided T test, pearson rank sum analysis, hidden markov model analysis, analysis of q-q plots, principal component analysis, one way ANOVA, two way ANOVA, LIMMA and the like.

[0201] In some embodiments of the present invention, the use of molecular profiling alone or in combination with cytological analysis may provide a diagnosis that is between about 85% accurate and about 99% or about 100% accurate. In some cases, the molecular profiling business may through the use of molecular profiling and/or cytology provide a diagnosis of malignant, benign, or normal that is about 85%, 86%, 87%, 88%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 97.5%, 98%, 98.5%, 99%, 99.5%, 99.75%, 99.8%, 99.85%, or 99.9% accurate.

[0202] In some cases, accuracy may be determined by tracking the subject over time to determine the accuracy of the original diagnosis. In other cases, accuracy may be established in a deterministic manner or using statistical methods. For example, receiver operator characteristic (ROC) analysis may be used to determine the optimal assay parameters to achieve a specific level of accuracy, specificity, positive predictive value, negative predictive value, and/or false discovery rate. Methods for using ROC analysis in cancer diagnosis are known in the art and have been described for example in US Patent Application No. 2006/019615 herein incorporated by reference in its entirety.

[0203] In some embodiments of the present invention, gene expression products and compositions of nucleotides encoding for such products which are determined to exhibit the greatest difference in expression level or the greatest difference in alternative splicing between benign and normal, benign and malignant, or malignant and normal may be chosen for use as molecular profiling reagents of the present invention. Such gene expression products may be particularly useful by providing a wider dynamic range, greater signal to noise, improved diagnostic power, lower likelihood of false positives or false negative, or a greater statistical confidence level than other methods known or used in the art.

[0204] In other embodiments of the present invention, the use of molecular profiling alone or in combination with cytological analysis may reduce the number of samples scored as non-diagnostic by about 100%, 99%, 95%, 90%, 80%, 75%, 70%, 65%, or about 60% when compared to the use of standard cytological techniques known to the art. In some cases, the methods of the present invention may reduce the number of samples scored as intermediate or suspicious by about 100%, 99%, 98%, 97%, 95%, 90%, 85%, 80%, 75%, 70%, 65%, or about 60%, when compared to the standard cytological methods used in the art.

[0205] In some cases the results of the molecular profiling assays, are entered into a database for access by representatives or agents of the molecular profiling business, the individual, a medical provider, or insurance provider. In some cases assay results include interpretation or diagnosis by a representative, agent or consultant of the business, such as a medical professional. In other cases, a computer or algorithmic analysis of the data is provided automatically. In some cases the molecular profiling business may bill the individual, insurance provider, medical provider, researcher, or government entity for one or more of the following: molecular profiling assays performed, consulting services, data analysis, reporting of results, or database access.

[0206] In some embodiments of the present invention, the results of the molecular profiling are presented as a report on a computer screen or as a paper record. In some cases, the report may include, but is not limited to, such information as one or more of the following: the number of genes differentially expressed, the suitability of the original sample, the number of genes showing differential alternative splicing, a

diagnosis, a statistical confidence for the diagnosis, the likelihood of cancer or malignancy, and indicated therapies.

[0207] (iv) Categorization of Samples Based on Molecular Profiling Results

[0208] The results of the molecular profiling may be classified into one of the following: benign (free of a cancer, disease, or condition), malignant (positive diagnosis for a cancer, disease, or condition), or non diagnostic (providing inadequate information concerning the presence or absence of a cancer, disease, or condition). In some cases, a diagnostic result may further classify the type of cancer, disease or condition. In other cases, a diagnostic result may indicate a certain molecular pathway involved in the cancer disease or condition, or a certain grade or stage of a particular cancer disease or condition. In still other cases a diagnostic result may inform an appropriate therapeutic intervention, such as a specific drug regimen like a kinase inhibitor such as Gleevec or any drug known to the art, or a surgical intervention like a thyroidectomy or a hemithyroidectomy.

[0209] In some embodiments of the present invention, results are classified using a trained algorithm. Trained algorithms of the present invention include algorithms that have been developed using a reference set of known malignant, benign, and normal samples including but not limited to the samples listed in FIG. **1**. Algorithms suitable for categorization of samples include but are not limited to k-nearest neighbor algorithms, concept vector algorithms, naive bayesian algorithms, neural network algorithms, hidden markov model algorithms, genetic algorithms, and mutual information feature selection algorithms or any combination thereof. In some cases, trained algorithms of the present invention may incorporate data other than gene expression or alternative splicing data such as but not limited to DNA polymorphism data, sequencing data, scoring or diagnosis by cytologists or pathologists of the present invention, information provided by the pre-classifier algorithm of the present invention, or information about the medical history of the subject of the present invention.

[0210] (v) Monitoring of Subjects or Therapeutic Interventions Via Molecular Profiling

[0211] In some embodiments, a subject may be monitored using methods and compositions of the present invention. For example, a subject may be diagnosed with cancer or a genetic disorder. This initial diagnosis may or may not involve the use of molecular profiling. The subject may be prescribed a therapeutic intervention such as a thyroidectomy for a subject suspected of having thyroid cancer. The results of the therapeutic intervention may be monitored on an ongoing basis by molecular profiling to detect the efficacy of the therapeutic intervention. In another example, a subject may be diagnosed with a benign tumor or a precancerous lesion or nodule, and the tumor, nodule, or lesion may be monitored on an ongoing basis by molecular profiling to detect any changes in the state of the tumor or lesion.

[0212] Molecular profiling may also be used to ascertain the potential efficacy of a specific therapeutic intervention prior to administering to a subject. For example, a subject may be diagnosed with cancer. Molecular profiling may indicate the upregulation of a gene expression product known to be involved in cancer malignancy, such as for example the RAS oncogene. A tumor sample may be obtained and cultured in vitro using methods known to the art. The application of various inhibitors of the aberrantly activated or dysregulated pathway, or drugs known to inhibit the activity of the pathway may then be tested against the tumor cell line for growth inhibition. Molecular profiling may also be used to monitor the effect of these inhibitors on for example down-stream targets of the implicated pathway.

[0213] (vi) Molecular Profiling as a Research Tool

[0214] In some embodiments, molecular profiling may be used as a research tool to identify new markers for diagnosis of suspected tumors; to monitor the effect of drugs or candidate drugs on biological samples such as tumor cells, cell lines, tissues, or organisms; or to uncover new pathways for oncogenesis and/or tumor suppression.

[0215] (vii) Biomarker Groupings Based on Molecular Profiling

[0216] Thyroid genes are described according to the groups 1) Benign vs. Malignant, 2) alternative gene splicing, 3) KEGG Pathways, 4) Normal Thyroid, 5) Thyroid pathology subtype, 6) Gene Ontology, and 7) Biomarkers of metastasis to the thyroid from non-thyroid organs. Methods and compositions of the invention can have genes selected from one or more of the groups listed above and/or 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50 or more subgroups from any of the groups listed above (e.g. one or more different KEGG pathway) and can have from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50 or more gene expression products from each group, in any combination. In some embodiments, the set of genes combined give a specificity or sensitivity of greater than 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 99.5%, or a positive predictive value or negative predictive value of at least 95%, 95.5%, 96%, 96.5%, 97%, 97.5%, 98%, 98.5%, 99%, 99.5% or more.

[0217] In some embodiments, the extracellular matrix, adherens, focal adhesion, and tight junction genes are used as biomarkers of thyroid cancer. In some embodiments, the signaling pathway is selected from one of the following three pathways: adherens pathway, focal adhesion pathway, and tight junction pathway. In some embodiments, at least one gene is selected from one of the 3 pathways. In some embodiments, at least one gene is selected from each one of the three pathways. In some embodiments, at least one gene is selected from two of the three pathways. In some embodiments, at least one gene that is involved in all three pathways is selected. In one example, a set of genes that is involved in adherens pathway, focal adhesion pathway, and tight junction pathway is selected as the markers for diagnosis of a cancer such as thyroid cancer.

[0218] The follicular cells that line thyroid follicles are highly polarized and organized in structure, requiring distinct roles of their luminal and apical cell membranes. In some embodiments, cytoskeleton, plasma membrane, and extracellular space genes are used as biomarkers of thyroid cancer. In some embodiments, genes that overlap all four pathways, i.e. ECM, focal adhesion, adherens, and tight junction pathways, are used as biomarkers of thyroid cancer. In one example, the present invention provides the Benign vs. malignant group (n=948) as a thyroid classification gene list. This list has been grouped according to alternative splicing, KEGG pathways, and gene ontology. KEGG pathways are further described in Table 1.

[0219] In some embodiments, the present invention provides a method of diagnosing cancer comprising gene expression products from one or more signaling pathways that include but are not limited to the following: acute

myeloid leukemia signaling, somatostatin receptor 2 signaling, cAMP-mediated signaling, cell cycle and DNA damage checkpoint signaling, G-protein coupled receptor signaling, integrin signaling, melanoma cell signaling, relaxin signaling, and thyroid cancer signaling. Methods and compositions of the invention can have genes selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50 or more signaling pathways and can have from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50 or more gene expression products from each signaling pathway, in any combination. In some embodiments, the set of genes combined give a specificity or sensitivity of greater than 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 99.5%, or a positive predictive value or negative predictive value of at least 95%, 95.5%, 96%, 96.5%, 97%, 97.5%, 98%, 98.5%, 99%, 99.5% or more.

[0220] In some embodiments, the present invention provides a method of diagnosing cancer comprising gene expression products from one or more ontology groups that include but are not limited to the following: cell aging, cell cortex, cell cycle, cell death/apoptosis, cell differentiation, cell division, cell junction, cell migration, cell morphogenesis, cell motion, cell projection, cell proliferation, cell recognition, cell soma, cell surface, cell surface linked receptor signal transduction, cell adhesion, transcription, immune response, or inflammation. Methods and compositions of the invention can have genes selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50 or more ontology groups and can have from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50 or more gene expression products from each ontology group, in any combination. In some embodiments, the set of genes combined give a specificity or sensitivity of greater than 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 99.5%, or a positive predictive value or negative predictive value of at least 95%, 95.5%, 96%, 96.5%, 97%, 97.5%, 98%, 98.5%, 99%, 99.5% or more.

TABLE 1

Genes involved in the KEGG Pathways

KEGG Pathway	% in Top 948 B vs. M list	Genes in Top 948 B vs. M list	Total Genes in Pathway
ECM	23	18	84
p53	14	10	69
PPAR	14	10	69
Thyroid Cancer	14	4	29
Focal Adhesion	13	26	201
Adherens	12	9	77
Tight Junction	11	14	134
Pathways in Cancer Overview	10	33	332
Jak/STAT	10	14	155
Cell Cycle	7	9	129
TGFbeta	7	6	87
Wnt	7	10	151
ErbB	6	5	87
Apoptosis	6	5	88
MAPK	5	14	269
Autoimmune Thyroid	4	2	53
mTOR	2	1	53
VEGF	1	1	76

[0221] Top Biomarkers of benign vs. malignant thyroid, n=948, are listed below in List 1:

List 1

[0222] TCID-2406391, TCID-3153400, TCID-3749600, ABCC3, ABCD2, ABTB2, ACBD7, ACSL1, ACTA2, ADAMTS5, ADAMTS9, ADK, ADORA1, AEBP1, AFAP1, AGR2, AHNAK2, AHR, AIDA, AIM2, AK1, AKR1C3, ALAS2, ALDH1A3, ALDH1B1, ALDH6A1, ALOX5, AMIGO2, AMOT, ANGPTL1, ANK2, ANKS6, ANO5, ANXA1, ANXA2, ANXA2P1, ANXA3, ANXA6, AOAH, AP3S1, APOBEC3F, APOBEC3G, APOL1, APOO, AQP4, AQP9, ARHGAP19, ARHGAP24, ARL13B, ARL4A, ARMCX3, ARMCX6, ARNTL, ARSG, ASAP2, ATIC, ATM, ATP13A4, ATP6V0D2, ATP8A1, AUTS2, AVPR1A, B3GNT3, BAGS, BCL2, BCL2A1, BCL9, BHLHE40, BHLHE41, BIRC5, BLNK, BMP1, BMP8A, BTBD11, BTG3, C10orf131, C10orf72, C11orf72, C11orf74, C11orf80, C12orf35, C12orf49, C14orf45, C16orf45, C17orf87, C19orf33, C1orf115, C1orf116, C2, C22orf9, C2orf40, C3, C4A, C4B, C4orf34, C4orf7, C5orf28, C6orf168, C6orf174, C7orf62, C8orf16, C8orf39, C8orf4, C8orf79, C9orf68, CA11, CADM1, CALCA, CAMK2N1, CAMK4, CAND1, CARD16, CARD17, CARD8, CASC5, CASP1, CAV1, CAV2, CCDC109B, CCDC121, CCDC146, CCDC148, CCDC152, CCDC80, CCL13, CCL19, CCND1, CCND2, CD151, CD180, CD2, CD200, CD36, CD3D, CD48, CD52, CD69, CD79A, CD96, CDCP1, CDH11, CDH3, CDH6, CDK2, CDKL2, CDO1, CDON, CDR1, CEP110, CEP55, CERKL, CFB, CFH, CFHR1, CFI, CHAF1B, CHD4, CHGB, CHI3L1, CITED1, CKB, CKS2, CLC, CLDN1, CLDN10, CLDN16, CLDN4, CLDN7, CLEC2B, CLEC4E, CLIP3, CLU, CMAH, CNN2, CNN3, COL12A1, COL1A1, COPZ2, CP, CPE, CPNE3, CR2, CRABP1, CRABP2, CSF3R, CSGALNACT1, CST6, CTNNAL1, CTNNB1, CTSC, CTSH, CTTN, CWH43, CXCL1, CXCL11, CXCL13, CXCL14, CXCL17, CXCL2, CXCL3, CXCL9, CXorf18, CXorf27, CYP1B1, CYP24A1, CYP27A1, CYP4B1, CYSLTR1, CYSLTR2, CYTH1, DAPK2, DCAF17, DCBLD2, DCUN1D3, DDAH1, DDB2, DDX52, DENND4A, DGKH, DGKI, DHRS1, DHRS3, DIO1, DIRAS3, DLC1, DLG2, DLG4, DLGAP5, DNAJB14, DNASE1L3, DOCK8, DOCK9, DOK4, DPH3B, DPP4, DPYD, DPYSL3, DSG2, DSP, DST, DUOX1, DUOX2, DUOXA1, DUOXA2, DUSP4, DUSP5, DUSP6, DYNC1I2, DYNLT1, DZIP1, ECE1, EDNRB, EFEMP1, EGF, EGFR, EHBP1, EHD2, EHF, EIF2B2, EIF4H, ELK3, ELMO1, EMP2, EMR3, ENAH, ENDOD1, ENTPD1, EPB41, EPDR1, EPHA4, EPHX4, EPR1, EPS8, ERBB2, ERBB3, ERI2, ERO1LB, ERP27, ESRRG, ETNK2, ETS1, ETV1, ETV4, ETV5, F2RL2, F8, FAAH2, FABP4, FAM111A, FAM111B, FAM164A, FAM176A, FAM20A, FAM55C, FAM82B, FAM84B, FAT4, FBLN5, FBXO2, FBXO21, FCN1, FCN2, FGF2, FGFR1OP2, FIBIN, FLJ20184, FLJ26056, FLJ32810, FLJ42258, FLRT3, FN1, FPR1, FPR2, FREM2, FRMD3, FXYD6, FYB, FZD4, FZD6, FZD7, G0S2, GABBR2, GABRB2, GADD45A, GALE, GALNT12, GALNT3, GALNT7, GBE1, GBP1, GBP3, GBP5, GGCT, GIMAP2, GIMAP5, GIMAP7, GJA4, GLA, GLDC, GLDN, GLIS3, GNG12, GOLT1A, GPAM, GPR110, GPR125, GPR155, GPR174, GPR98, GPRC5B, GRAMD3, GSN, GTF3A, GULP1, GYPB, GYPC, GYPE, GZMA, GZMK, HEMGN, HEY2, HIGD1A, HIPK2, HIST1H1A, HIST1H3B, HIST1H4L,

HK1, HLA-DPB1, HLA-DQB2, HLF, HMGA2, HMMR, HNRNPM, HPN, HPS3, HRASLS, HSD17B6, HSPH1, ICAM1, ID3, IFI16, IFITM1, IFNAR2, IGF2BP2, IGFBP5, IGFBP6, IGFBP7, IGJ, IGK, IGKC, IGKV1-5, IGKV3-15, IGKV3-20, IGKV3D-11, IGKV3D-15, IGSF1, IKZF2, IKZF3, IKZF4, IL1RAP, IL1RL1, IL2RA, IL7R, IL8, IL8RA, IL8RB, IL8RBP, IMPDH2, INPP5F, IPCEF1, IQGAP2, ISYNA1, ITGA2, ITGA3, ITGA4, ITGA9, ITGB1, ITGB4, ITGB6, ITGB8, ITM2A, ITPR1, IYD, JAK2, JUB, KAL1, KATNAL2, KBTBD8, KCNA3, KCNAB1, KCNK5, KCNQ3, KCTD14, KDELC1, KDELR3, KHDRBS2, KIAA0284, KIAA0408, KIAA1217, KIAA1305, KIF11, KIT, KLF8, KLHDC8A, KLHL6, KLK10, KLK7, KLRB1, KLRC4, KLRG1, KLRK1, KRT18, KRT19, KYNU, LAMB1, LAMB3, LAMC1, LAMC2, LCA5, LCMT1, LCN2, LCP1, LDOC1, LEMD1, LGALS2, LGALS3, LIFR, LILRA1, LILRB1, LIMA1, LINGO2, LIPH, LMO3, LMO4, LOC100124692, LOC100127974, LOC100129112, LOC100129115, LOC100129171, LOC100129961, LOC100130100, LOC100130248, LOC100131102, LOC100131490, LOC100131869, LOC100131938, LOC100131993, LOC100132338, LOC100132764, LOC26080, LOC283508, LOC284861, LOC439911, LOC440434, LOC440871, LOC554202, LOC643454, LOC646358, LOC648149, LOC650405, LOC652493, LOC652694, LOC653264, LOC653354, LOC653498, LOC728212, LOC729461, LOC730031, LONRF2, LOX, LPAR1, LPAR5, LPCAT2, LPL, LRP1B, LRP2, LRRC69, LRRN1, LRRN3, LTBP2, LTBP3, LUM, LYPLA1, LYRM1, LYZ, MACC1, MAFG, MAGOH2, MAMLD1, MAP2, MAPK4, MAPK6, MATN2, MBOAT2, MCM4, MCMI, MDK, ME1, MED13, MED13L, MELK, MET, METTL7B, MEX3C, MFGE8, MGAM, MGAT1, MGAT4C, MGC2889, MGST1, MIS12, MKI67, MLLT3, MLLT4, MMP16, MNDA, MORC4, MPPED2, MPZL2, MRC2, MRPL14, MT1F, MT1G, MT1H, MT1M, MT1P2, MT1P3, MTHFD1L, MTIF3, MUC1, MUC15, MVP, MXRA5, MYEF2, MYH10, MYO1B, MYO1D, MYO5A, MYO6, NAB2, NAE1, NAG20, NAV2, NCAM1, NCKAP1, ND1, NDC80, NDFIP2, NEB, NEDD4L, NELL2, NEXN, NFATC3, NFE2, NFIB, NFKBIZ, NIPAL3, NIPSNAP3A, NIPSNAP3B, NOD1, NPAS3, NPAT, NPC2, NPEPPS, NPL, NPY1R, NRCAM, NRIP1, NRP2, NT5E, NTAN1, NUCB2, NUDT6, NUPR1, NUSAP1, OCIAD2, OCR1, ODZ1, ORAOV1, OSBPL1A, OSGEP, OSMR, P2RY13, P4HA2, PAM, PAPSS2, PARD6B, PARP14, PARP4, PARVA, PBX1, PCDH1, PCMTD1, PCNXL2, PDE5A, PDE9A, PDGFRL, PDK4, PDLIM1, PDLIM4, PDZRN4, PEG10, PERP, PGCP, PHEX, PHF16, PHLDB2, PHYHIP, PIAS3, PIGN, PKHD1L1, PKP2, PKP4, PLA2G16, PLA2G7, PLA2R1, PLAG1, PLAU, PLCD3, PLCL1, PLEK, PLEKHA4, PLEKHA5, PLEKHF2, PLK2, PLP2, PLS3, PLSCR4, PLXNC1, PMEPA1, POLR2J4, PON2, POR, POU2F3, PPAP2C, PPARGC1A, PPBP, PPL, PPP1R14C, PRCP, PRICKLE1, PRINS, PRMT6, PROK2, PROS1, PRR15, PRRG1, PRSS23, PSAT1, PSD3, PTK7, PTPN14, PTPN22, PTPRC, PTPRE, PTPRF, PTPRG, PTPRK, PTPRU, PTRF, PXDNL, PYGL, PYHIN1, QTRT1, RAB25, RAB27A, RAB32, RAB34, RAD23B, RAG2, RAI2, RAPGEF5, RARG, RASA1, RASD2, RBBP7, RBBP8, RBMS2, RCBTB2, RCE1, RDH5, RG9MTD2, RGS13, RGS18, RGS2, RHOBTB3, RHOH, RHOU, RICH2, RIMS2, RNASE1, RNASET2, RND3, ROS1, RPL39L, RPL9P11, RPRD1A, RPS6KA6, RRAS, RRAS2, RRBP1, RRM2, RUNX1, RUNX2, RXRG, RYR2, S100A12, S100A14, S100A16, S100A8, S100A9, SALL1, SAV1, SC4MOL, SCARA3, SCARNA11, SCEL, SCG3, SCG5, SCNN1A, SCP2, SCRN1, SDC4, SDK1, SEH1L, SEL1L3, SELL, SEMA3C, SEMA3D, SEMA4C, SEPP1, SEPT11, SERGEF, SERINC2, SERPINA1, SERPINA2, SERPINE2, SERPING1, SFN, SFTPB, SGCB, SGCE, SGEF, SGMS2, SGPP2, SH2D4A, SH3BGR, SH3PXD2A, SIPA1L2, SIRPA, SIRPB1, SLA, SLC12A2, SLC16A4, SLC16A6, SLC17A5, SLC24A5, SLC25A33, SLC26A4, SLC26A7, SLC27A2, SLC27A6, SLC34A2, SLC35D2, SLC35F2, SLC39A6, SLC4A4, SLC5A8, SLC7A11, SLC7A2, SLIT1, SLIT2, SLPI, SMAD9, SMOC2, SMURF2, SNCA, SNX1, SNX22, SNX7, SOAT1, SORBS2, SP140, SP140L, SPATS2, SPATS2L, SPC25, SPINT1, SPOCK1, SPP1, SPRED2, SPRY1, SPRY2, SQLE, SRL, SSPN, ST20, ST3GAL5, STAT4, STEAP2, STK17B, STK32A, STXBP6, SULF1, SYNE1, SYT14, SYTL5, TACSTD2, TASP1, TBC1D3F, TC2N, TCERG1L, TCF7L2, TCFL5, TDRKH, TEAD1, TFCP2L1, TFF3, TFPI, TGFA, TGFB2, TGFBR1, THSD4, TIAM2, TIMP1, TIMP3, TIPARP, TJP1, TJP2, TLCD1, TLE4, TLR10, TLR8, TM4SF1, TM4SF4, TM7SF4, TMEM100, TMEM117, TMEM133, TMEM156, TMEM163, TMEM171, TMEM215, TMEM220, TMEM90A, TMEM98, TMPRSS4, TMSB10, TMSB15A, TMSB15B, TNC, TNFAIP8, TNFRSF11B, TNFRSF12A, TNFRSF17, TNFSF10, TNFSF15, TOMM34, TOX, TPD52L1, TPO, TPX2, TRIP10, TRPC5, TRPC6, TSC22D1, TSHZ2, TSPAN13, TSPAN6, TSPAN8, TSSC1, TTC39A, TUBB1, TUBB6, TULP3, TUSC3, TXNL1, TXNRD1, TYMS, UCHL5, VAMP1, VNN1, VNN2, VNN3, WDR40A, WDR54, WDR72, WIPI1, WNT5A, XKRX, XPR1, YIF1B, YIPF1, YTHDC2, ZBTB33, ZCCHC12, ZCCHC16, ZEB2, ZFP36L1, ZFPM2, ZMAT3, ZMAT4, ZNF143, ZNF208, ZNF487, ZNF643, ZNF804B, ZYG11A.

[0223] Alternative spliced genes, n=283, are listed below in List 2:

List 2

[0224] ABCC3, ADAMTS5, ADAMTS9, AIDA, AK1, AKR1C3, ALDH1A3, ALDH6A1, AMIGO2, AMOT, ANGPTL1, ANKS6, ANO5, ANXA1, ANXA2, ANXA2P1, ANXA3, AQP4, ARHGAP24, ARL4A, ARMCX3, ARMCX6, ARSG, ATIC, ATP13A4, ATP8A1, AUTS2, BAGS, BCL2, BCL9, BHLHE41, C10orf131, C11orf74, C14orf45, C16orf45, C19orf33, C2orf40, C3, C5orf28, C8orf79, CA11, CALCA, CAV1, CCND1, CCND2, CD36, CD36, CDH3, CDH6, CDON, CFH, CFHR1, CHD4, CITED1, CLDN16, CLU, COPZ2, CP, CRABP1, CSGALNACT1, CTSC, CTSH, CTTN, CWH43, CYSLTR2, DCBLD2, DCUN1D3, DDB2, DGKH, DGKI, DIO1, DLG2, DOCK9, DPH3B, DPP4, DSP, DST, DUSP6, EFEMP1, EIF2B2, ELMO1, EMP2, ENAH, ENTPD1, EPHX4, ERBB3, ERI2, ERO1LB, ETNK2, ETV1, ETV5, F8, FABP4, FAM111B, FAM20A, FAM55C, FAT4, FBLN5, FGFR1OP2, FLJ42258, FLRT3, FN1, FREM2, FXYD6, GABBR2, GABRB2, GALNT7, GBE1, GBP1, GBP3, GGCT, GIMAP7, GPAM, GPR125, GPR155, GRAMD3, GSN, HLF, HMGA2, HSPH1, IMPDH2, IQGAP2, ITGA2, ITGA3, ITGA9, ITGB6, ITGB8, ITM2A, ITPR1, IYD, KATNAL2, KCNA3, KCNQ3, KDELC1, KHDRBS2, KIAA0284, KIAA1217, KIT, KLF8, KLK10, KRT19,

LAMB3, LAMC2, LEMD1, LIFR, LINGO2, LMO3, LOC100127974, LOC100129112, LOC100131490, LOC100131869, LOC283508, LOC648149, LOC653354, LONRF2, LPCAT2, LPL, LRP1B, LRP2, LRRC69, LRRN1, LRRN3, LYRM1, MACC1, MAFG, MAP2, MAPK4, MAPK6, MATN2, MED13, MET, METTL7B, MFGE8, MLLT3, MPPED2, MPZL2, MRPL14, MT1F, MT1G, MT1H, MT1P2, MTHFD1L, MUC1, MVP, MYEF2, MYH10, MYO1D, NAG20, NAV2, NEB, NEDD4L, NELL2, NFATC3, NFKBIZ, NPC2, NRCAM, NUCB2, ORAOV1, P4HA2, PAM, PAPSS2, PARVA, PDLIM4, PEG10, PGCP, PIGN, PKHD1L1, PLA2G16, PLA2G7, PLA2R1, PLAU, PLEKHA4, PLP2, PLSCR4, PLXNC1, PMEPA1, PON2, PPARGC1A, PRINS, PROS1, PSD3, PTPRK, PYHIN1, QTRT1, RAB27A, RAB34, RAD23B, RASA1, RHOBTB3, RNASET2, RPS6KA6, RUNX1, SCARNA11, SCG5, SDC4, SERPINA1, SERPINA2, SGEF, SH2D4A, SLA, SLC12A2, SLC24A5, SLC26A4, SLC26A7, SLC27A2, SLC27A6, SLC35F2, SLC4A4, SLC5A8, SLC7A2, SOAT1, SPATS2, SPATS2L, SPINT1, SPP1, SSPN, STK32A, SULF1, SYNE1, TCFL5, TFPI, TGFBR1, TIPARP, TJP1, TLE4, TM7SF4, TMEM171, TMEM90A, TNFAIP8, TNFRSF11B, TOMM34, TPD52L1, TPO, TSC22D1, TUSC3, TYMS, WDR54, WDR72, WIPI1, XPR1, YIF1B, ZFPM2, ZMAT4.

[0225] Genes involved in the KEGG pathways are listed below in Table 6: there are 18 pathways with a total of n=109 unique genes.

TABLE 6

Signaling Pathway	Number of Genes	Genes
ECM Pathway	19	CD36, COL1A1, FN1, HMMR, ITGA2, ITGA3, ITGA4, ITGA9, ITGB1, ITGB4, ITGB6, ITGB8, LAMB1, LAMB3, LAMC1, LAMC2, SDC4, SPP1, TNC
p53 Pathway	10	ATM, CCND1, CCND2, CDK2, DDB2, GADD45A, PERP, RRM2, SFN, ZMAT3
PPAR Pathway	10	ACSL1, CD36, CYP27A1, FABP4, LPL, ME1, RXRG, SCP2, SLC27A2, SLC27A6
Thyroid Cancer Pathway	4	CCND1, CTNNB1, RXRG, TCF7L2
Focal Adhesion Pathway	26	BCL2, CAV1, CAV2, CCND1, CCND2, COL1A1, CTNNB1, EGF, EGFR, ERBB2, FN1, ITGA2, ITGA3, ITGA4, ITGA9, ITGB1, ITGB6, ITGB8, LAMB1, LAMB3, LAMC1, LAMC2, MET, PARVA, SPP1, TNC
Adherens Pathway	9	CTNNB1, EGFR, ERBB2, MET, MLLT4, PTPRF, TCF7L2, TGFBR1, TJP1
Tight Junctions Pathway	15	CLDN1, CLDN10, CLDN16, CLDN4, CLDN7, CTNNB1, CTTN, EPB41, MLLT4, MYH10, PARD6B, RRAS, RRAS2, TJP1, TJP2
Pathways in Cancer Overview	34	BCL2, BIRC5, CCND1, CDK2, CSF3R, CTNNB1, DAPK2, EGF, EGFR, ERBB2, ETS1, FGF2, FN1, FZD4, FZD6, FZD7, IL8, ITGA2, ITGA3, ITGB1, KIT, LAMB1, LAMB3, LAMC1, LAMC2, MET, PIAS3, RUNX1, RXRG, TCF7L2, TGFA, TGFB2, TGFBR1, WNT5A

TABLE 6-continued

Signaling Pathway	Number of Genes	Genes
Jak/STAT Pathway	16	CCND1, CCND2, CSF3R, IFNAR2, IL2RA, IL7R, ITGB4, JAK2, LIFR, OSMR, PIAS3, SPRED2, SPRY1, SPRY2, STAT4, TPO
Cell Cycle Pathway	9	ATM, CCND1, CCND2, CDK2, GADD45A, MCM4, MCM7, SFN, TGFB2
TGFbeta Pathway	6	BMP8A, ID3, SMAD9, SMURF2, TGFB2, TGFBR1
Wnt Pathway	10	CCND1, CCND2, CTNNB1, FZD4, FZD6, FZD7, NFATC3, PRICKLE1, TCF7L2, WNT5A
Erb Pathway	5	EGF, EGFR, ERBB2, ERBB3, TGFA
Apoptosis Pathway	5	ATM, BCL2, ENDOD1, IL1RAP, TNFSF10
MAPK Pathway	14	DUSP4, DUSP5, DUSP6, EGF, EGFR, FGF2, GADD45A, GNG12, RASA1, RPS6KA6, RRAS, RRAS2, TGFB2, TGFBR1
Autoimmune Thyroid pathway	2	HLA-DPB1, TPO
mTOR Pathway	1	RPS6KA6
VEGF Pathway	1	NFATC3

[0226] Top genes separating benign and malignant thyroid (combined) from normal thyroid, n=55, are listed below in List 3:

List 3

[0227] ANGPTL1, ANXA3, C10orf131, C2orf40, C7orf62, CAV1, CCDC80, CDR1, CFH, CFHR1, CLDN16, CP, CRABP1, EFEMP1, ENTPD1, FABP4, FBLN5, FN1, GBP1, GBP3, GULP1, HSD17B6, IPCEF1, KIT, LRP1B, LRRC69, LUM, MAPK6, MATN2, MPPED2, MT1F, MT1G, MT1H, MT1M, MT1P2, MT1P3, MYEF2, NRCAM, ODZ1, PAPSS2, PKHD1L1, PLA2R1, RYR2, SEMA3D, SLC24A5, SLC26A4, SLC26A7, SLIT2, TFPI, TMEM171, TPO, TSPAN8, YTHDC2, ZFPM2, ZNF804B.

[0228] Thyroid surgical pathology subtypes, n=873, are listed below:

[0229] (i) List 4: FA Subtype, n=243:

[0230] TCID-3124344, AHR, ALOX5, ANGPTL1, ANXA2, ANXA2P1, APOL1, AVPR1A, BMP8A, BTBD11, C2, C3, C8orf39, CCDC109B, CD36, CDON, CFB, CHGB, CHI3L1, CKB, CLDN1, CP, CRABP1, CTSC, CTSH, CXCL1, CXCL2, CXCL3, CXorf27, CYP1B1, DLG2, DNASE1L3, DPP4, DUOX1, DUOX2, DYNLT1, EIF4H, F8, FABP4, FAM20A, FAM55C, FBLN5, FLJ26056, FXYD6, G0S2, GALNT7, GLIS3, GPAM, HIGD1A, HK1, HLF, HSD17B6, ICAM1, IGFBP7, IL1RAP, IPCEF1, IYD, KATNAL2, KCNAB1, KHDRBS2, KLF8, KLHDC8A, LAMB1, LGALS3, LOC100131869, LOC26080, LOC284861, LOC439911, LOC653264, LOC728212, LOC729461, LPCAT2, LRRC69, MAGOH2, MAPK4, MAPK6, MELK, MPPED2, MT1G, NEB, NFKBIZ, NRIP1, PARP14, PKHD1L1, PLA2G7, PLP2, PLXNC1, POR, PRMT6, PROS1, PSMB2, PTPRE, PYGL, RNASE1, RNASET2, RPL9P11, RRAS2, RRBP1, RUNX1, RUNX2, RYR2, SCP2, SEL1L3, SERGEF, SGPP2, SH3BGR, SLC25A33, SLC26A4, SLC26A7, SLC27A6, SLC4A4, SLPI, SORBS2, SQLE, STK32A, SYTL5, TFCP2L1, TIAM2, TIMP3, TMEM220, TMSB10, TRPC6, TSHZ2,

TSSC1, VAMP1, ZNF487, ABCC3, C11orf72, C8orf79, CLDN16, CLU, CST6, CYSLTR2, DIO1, DPH3B, ERO1LB, FN1, GABRB2, IGFBP6, IKZF3, KIT, KRT19, LIFR, LIPH, MACC1, MAFG, MPZL2, MT1F, MT1H, MT1P2, NELL2, ODZ1, RAG2, ROS1, SERPINA1, SERPINA2, SLC34A2, TCFL5, TIMP1, TPO, ZMAT4, ADAMTS9, ALDH1B1, ALDH6A1, ANO5, APOO, C10orf72, C11orf74, C14orf45, C2orf40, C4A, C4B, C5orf28, C6orf174, CAMK2N1, CCDC121, CCND1, CDH3, CITED1, COPZ2, CPNE3, CRABP2, CSGALNACT1, DAPK2, DLC1, ECE1, EIF2B2, EMP2, ERBB2, FAM82B, FIBIN, FLJ42258, FRMD3, HEY2, HRASLS, ID3, IGF2BP2, IGSF1, IKZF2, ITGA9, KIAA0408, KIAA1305, LMO3, MATN2, MDK, MET, METTL7B, MFGE8, MGC2889, MIS12, NAV2, NCAM1, NIPSNAP3A, NIPSNAP3B, NOD1, NTAN1, NUCB2, NUPR1, PCMTD1, PIGN, PLAG1, PSAT1, PXDNL, QTRT1, RG9MTD2, RXRG, SDC4, SLC35D2, SLC7A11, SMAD9, SPRY1, STEAP2, TASP1, TCF7L2, TMEM171, TNFRSF11B, TNFRSF12A, TRPC5, TXNL1, WDR72, YIPF1, ZCCHC12, ZCCHC16.

[0231] (ii) List 5: FC Subtype, n=102:

[0232] TCID-3124344, ABCC3, ANGPTL1, AVPR1A, C8orf39, CD2, CD36, CD48, CD52, CKB, CLDN1, CLDN16, CRABP1, CXCL9, DIO1, DLG2, DNASE1L3, DPH3B, DYNLT1, EIF4H, ERO1LB, F8, FABP4, FBLN5, FLJ26056, FXYD6, FYB, GLIS3, GULP1, GZMA, GZMK, HK1, HLA-DPB1, IFITM1, IGFBP7, IGJ, IGK@, IGKC, IGKV1-5, IGKV3-15, IGKV3-20, IGKV3D-11, IGKV3D-15, IPCEF1, KHDRBS2, KLHDC8A, KLRC4, KLRK1, LAMB1, LCP1, LIFR, LOC100130100, LOC100131869, LOC26080, LOC284861, LOC439911, LOC440871, LOC650405, LOC652493, LOC652694, LOC653264, LOC728212, LOC729461, LYZ, MAGOH2, MAPK4, MT1F, MT1H, MT1P2, NEB, ODZ1, PLA2G7, POR, PRMT6, PSMB2, PTPRC, RAG2, RNASE1, RNASET2, RPL9P11, RRAS2, RRBP1, RYR2, SCP2, SERGEF, SGPP2, SH3BGR, SLC25A33, SLC26A4, SQLE, STK32A, TCFL5, TFCP2L1, TIAM2, TIMP3, TMEM220, TPO, TRPC6, TSSC1, VAMP1, ZFPM2, ZNF487.

[0233] (iii) List 6: LCT Subtype, n=140:

[0234] ADAMTS9, AIM2, APOBEC3F, APOBEC3G, ARHGAP19, ATP13A4, BAG3, BCL2A1, BIRC5, BLNK, C10orf72, C11orf72, C12orf35, C4orf7, C6orf168, CALCA, CARD17, CARD8, CASP1, CCL19, CCND1, CD180, CD2, CD3D, CD48, CD52, CD79A, CD96, CEP110, CHGB, CLDN16, CLEC2B, CNN2, COL12A1, CR2, CXCL13, CXCL9, CYTH1, DENND4A, DNAJB14, DOCK8, DPYD, DUOX1, DUOX2, DUOXA1, DUOXA2, DUSP6, DYNC1I2, EGF, EPDR1, EPR1, EPS8, ETS1, FLJ42258, FYB, GABBR2, GABRB2, GALNT7, GBP5, GIMAP2, GIMAP5, GIMAP7, GPR155, GPR174, GTF3A, GZMA, GZMK, HIST1H3B, HIST1H4L, HLA-DPB1, HNRNPM, IFI16, IFITM1, IFNAR2, IGF2BP2, IGJ, IGK@, IGKC, IGKV1-5, IGKV3-15, IGKV3-20, IGKV3D-11, IGKV3D-15, IKZF3, IL7R, ITM2A, JAK2, KBTBD8, KLHL6, KLRC4, KLRG1, KLRK1, KYNU, LCP1, LIPH, LOC100130100, LOC100131490, LOC440871, LOC646358, LOC650405, LOC652493, LOC652694, LONRF2, LYZ, MED13L, METTL7B, MPZL2, MTIF3, NAV2, ND1, NFATC3, ODZ1, PAPSS2, PROS1, PSD3, PTPRC, PYGL, PYHIN1, RAD23B, RGS13, RIMS2, RRM2, SCG3, SLIT1, SP140, SP140L, SPC25, ST20, ST3GAL5, STAT4, STK32A, TC2N, TLE4, TNFAIP8, TNFRSF17, TNFSF10, TOX, UCHL5, ZEB2, ZNF143.

[0235] (iv) List 7: FVPTC Subtype, n=182:

[0236] ABCC3, ADAMTS9, AIDA, ALDH1B1, ALDH6A1, ANK2, ANO5, APOL1, APOO, AQP4, ATP13A4, BMP8A, C10orf72, C11orf72, C11orf74, C12orf35, C14orf45, C2orf40, C4A, C4B, C5orf28, C6orf174, C8orf79, CAMK2N1, CCDC121, CCND1, CCND2, CD36, CDH3, CITED1, CLDN1, CLDN16, CLDN4, CLEC2B, CLU, COPZ2, CPNE3, CRABP2, CSGALNACT1, CST6, CWH43, CYSLTR2, DAPK2, DCAF17, DIO1, DIRAS3, DLC1, DOCK9, DPH3B, DUOX1, DUOX2, DUOXA1, DUOXA2, DUSP6, ECE1, EIF2B2, EMP2, ERBB2, ERO1LB, ESRRG, FABP4, FAM82B, FAT4, FIBIN, FLJ42258, FN1, FRMD3, GABBR2, GABRB2, GIMAP2, GIMAP7, GPR155, GPR98, GTF3A, GZMA, GZMK, HEY2, HRASLS, ID3, IGF2BP2, IGFBP6, IGSF1, IKZF2, IKZF3, ITGA9, JAK2, KIAA0284, KIAA0408, KIAA1217, KIAA1305, KIT, KLRC4, KLRK1, KRT19, LGALS3, LIFR, LIPH, LMO3, LOC100131490, LOC100131993, LRP1B, LRP2, MACC1, MAFG, MAPK6, MATN2, MDK, MET, METTL7B, MFGE8, MGC2889, MIS12, MPPED2, MPZL2, MT1F, MT1G, MT1H, MT1P2, MTIF3, NAV2, NCAM1, NELL2, NFATC3, NIPSNAP3A, NIPSNAP3B, NOD1, NRCAM, NTAN1, NUCB2, NUPR1, ODZ1, PCMTD1, PDE5A, PIGN, PKHD1L1, PLA2R1, PLAG1, PLSCR4, PRINS, PSAT1, PXDNL, QTRT1, RAG2, RCBTB2, RG9MTD2, ROS1, RPS6KA6, RXRG, SALL1, SCG5, SDC4, SERPINA1, SERPINA2, SLC26A4, SLC34A2, SLC35D2, SLC7A11, SMAD9, SPRY1, ST3GAL5, STEAP2, STK32A, TASP1, TCF7L2, TCFL5, TIMP1, TMEM171, TMEM215, TNFAIP8, TNFRSF11B, TNFRSF12A, TNFSF10, TPO, TRPC5, TXNL1, UCHL5, WDR72, YIPF1, ZCCHC12, ZCCHC16, ZMAT4, ZYG11A.

[0237] (v) List 8: PTC Subtype, n=604:

[0238] TCID-3153400, TCID-3749600, ABCC3, ABTB2, ACBD7, ACSL1, ACTA2, ADAMTS5, ADAMTS9, ADK, AGR2, AHNAK2, AHR, AIDA, AK1, ALAS2, ALDH1A3, ALOX5, AMIGO2, AMOT, ANK2, ANXA1, ANXA2, ANXA2P1, ANXA3, AOAH, AP3S1, APOL1, AQP9, ARHGAP24, ARL13B, ARL4A, ARMCX3, ARMCX6, ARNTL, ASAP2, ATIC, ATP13A4, ATP13A4, B3GNT3, BCL9, BHLHE40, BHLHE41, BMP8A, BTBD11, BTG3, C11orf72, C11orf80, C12orf49, C16orf45, C19orf33, C1orf115, C1orf116, C2, C2orf40, C3, C4A, C4B, C4orf34, C6orf168, C6orf174, C7orf62, C8orf4, C8orf79, CA11, CADM1, CAMK2N1, CAND1, CAV1, CAV2, CCDC109B, CCDC121, CCDC148, CCDC80, CCL13, CCND1, CCND2, CD151, CD200, CD36, CDCP1, CDH11, CDH3, CDH6, CDK2, CDKL2, CDO1, CDON, CDR1, CFB, CFH, CFHR1, CFI, CHAF1B, CHD4, CHI3L1, CITED1, CKS2, CLC, CLDN1, CLDN10, CLDN16, CLDN4, CLDN7, CLEC4E, CLU, CNN3, COL1A1, CP, CRABP1, CRABP2, CSF3R, CST6, CTNNAL1, CTNNB1, CTSC, CTSH, CTTN, CXCL1, CXCL14, CXCL17, CXCL2, CXCL3, CXorf18, CXorf27, CYP1B1, CYSLTR2, DAPK2, DCBLD2, DCUN1D3, DDAH1, DDB2, DDX52, DGKH, DGKI, DHRS1, DHRS3, DIO1, DIRAS3, DLC1, DOCK9, DPP4, DPYSL3, DSG2, DSP, DST, DUSP4, DUSP5, DUSP6, DZIP1, ECE1, EDNRB, EGFR, EHBP1, EHD2, EHF, ELKS, ELMO1, EMP2, EMR3, ENAH, ENDOD1, EPB41, EPHA4, EPHX4, EPS8, ERBB3, ERI2, ERP27, ESRRG, ETNK2, ETV1, ETV5, F2RL2, FAAH2, FABP4,

FAM111A, FAM111B, FAM164A, FAM176A, FAM20A, FAM55C, FAM84B, FBXO2, FBXO21, FCN1, FCN2, FGF2, FGFR1OP2, FLJ20184, FLJ32810, FLJ42258, FLRT3, FN1, FPR1, FPR2, FRMD3, FZD4, FZD6, FZD7, G0S2, GABBR2, GABRB2, GADD45A, GALE, GALNT12, GALNT3, GALNT7, GBP1, GBP3, GGCT, GLDN, GNG12, GOLT1A, GPAM, GPR110, GPR110, GPR125, GPR98, GPRC5B, GRAMD3, GSN, GYPB, GYPC, GYPE, HEMGN, HEY2, HIGD1A, HIST1H1A, HLA-DQB2, HLF, HMGA2, HPN, HSPH1, ICAM1, IGF2BP2, IGFBP5, IGFBP6, IGSF1, IKZF3, IL1RAP, IL1RL1, IL8RA, IL8RB, IL8RB, IL8RBP, IL8RBP, IMPDH2, INPP5F, IPCEF1, IQGAP2, ITGA2, ITGA3, ITGA9, ITGB1, ITGB6, ITGB8, ITPR1, JUB, KAL1, KAT-NAL2, KCNK5, KCNQ3, KCTD14, KDELC1, KDELR3, KHDRBS2, KIAA0284, KIAA0408, KIAA1217, KIT, KLF8, KLK10, KLK7, KRT18, KRT19, LAMB3, LAMC1, LAMC2, LCA5, LCMT1, LCN2, LDOC1, LEMD1, LGALS3, LILRA1, LILRB1, LIMA1, LINGO2, LIPH, LMO3, LMO4, LOC100124692, LOC100127974, LOC100129112, LOC100129115, LOC100129171, LOC100129961, LOC100130248, LOC100131102, LOC100131490, LOC100131938, LOC100132338, LOC100132764, LOC283508, LOC440434, LOC554202, LOC643454, LOC648149, LOC653354, LOC653498, LOC730031, LONRF2, LOX, LPAR5, LPL, LRP1B, LRP2, LRRC69, LRRN1, LUM, LYRM1, MACC1, MAFG, MAMLD1, MAP2, MAPK6, MATN2, MBOAT2, MCM4, MCMI, MDK, MED13, MET, METTL7B, MEX3C, MFGE8, MGAM, MGAT4C, MGST1, MLLT4, MMP16, MMP16, MNDA, MORC4, MPPED2, MPZL2, MRPL14, MT1F, MT1G, MT1H, MT1M, MT1P2, MT1P3, MTHFD1L, MUC1, MUC15, MVP, MXRA5, MYEF2, MYH10, MYO1B, MYO1D, MYO6, NAB2, NAE1, NAG20, NCKAP1, NDFIP2, NEDD4L, NELL2, NEXN, NFE2, NFIB, NFKBIZ, NIPAL3, NOD1, NPC2, NPEPPS, NPY1R, NRCAM, NRIP1, NRP2, NT5E, NUDT6, OCIAD2, OCR1, ODZ1, OSGEP, OSMR, P2RY13, P4HA2, PAM, PARP14, PARP4, PARVA, PBX1, PDE5A, PDE9A, PDGFRL, PDLIM1, PDLIM4, PDZRN4, PEG10, PERP, PHEX, PHF16, PHLDB2, PHYHIP, PKHD1L1, PKP4, PLA2G16, PLA2R1, PLAG1, PLAU, PLCD3, PLE-KHA4, PLEKHA5, PLK2, PLP2, PLS3, PLXNC1, PMEPA1, PON2, PPARGC1A, PPBP, PPL, PPP1R14C, PRICKLE1, PRINS, PROK2, PROS1, PRR15, PRRG1, PRSS23, PSD3, PTPN14, PTPRE, PTPRF, PTPRG, PTPRK, PTRF, QTRT1, RAB25, RAB27A, RAB34, RAD23B, RAG2, RAI2, RAPGEF5, RARG, RASA1, RASD2, RBBP7, RBBP8, RBMS2, RCE1, RDH5, RGS18, RGS2, RHOU, RND3, ROS1, RPL39L, RPRD1A, RPS6KA6, RRAS, RUNX1, RUNX2, RXRG, S100A12, S100A14, S100A16, S100A8, S100A9, SALL1, SAV1, SC4MOL, SCARA3, SCARNA11, SCEL, SCG5, SCNN1A, SCRN1, SDC4, SEH1L, SEL1L3, SELL, SEMA3D, SEPT11, SERINC2, SERPINA1, SERPINA2, SERPINE2, SERPING1, SFN, SFTPB, SGCB, SGCE, SGEF, SGMS2, SH2D4A, SH3PXD2A, SIRPA, SIRPB1, SLA, SLC12A2, SLC16A4, SLC17A5, SLC24A5, SLC26A4, SLC26A7, SLC27A2, SLC27A6, SLC34A2, SLC35F2, SLC39A6, SLC4A4, SLC5A8, SLC7A2, SLIT2, SLPI, SMOC2, SMURF2, SNCA, SNX1, SNX22, SNX7, SORBS2, SPATS2, SPATS2L, SPINT1, SPRED2, SPRY1, SPRY2, SRL, SSPN, ST3GAL5, STK32A, SULF1, SYNE1, SYT14, SYTL5, TACSTD2, TBC1D3F, TDRKH, TEAD1, TEAD1, TFCP2L1, TFF3, TGFA, TGFB2, TGFBR1, TIMP1, TIPARP, TJP1, TJP2, TLCD1, TLR8, TM4SF1, TM4SF4, TM7SF4, TMEM100, TMEM117, TMEM133, TMEM163, TMEM215, TMEM90A, TMEM98, TMPRSS4, TMSB10, TNC, TNFRSF12A, TNFSF15, TOMM34, TPD52L1, TPO, TRIP10, TRPC5, TSC22D1, TSPAN13, TSPAN6, TUBB1, TUBB6, TULP3, TUSC3, TYMS, VNN2, VNN3, WDR40A, WDR54, WNT5A, XKRX, XPR1, YIF1B, YTHDC2, ZBTB33, ZCCHC12, ZCCHC16, ZFP36L1, ZMAT3, ZMAT4, ZNF643, ZNF804B.

[0239] (vi) List 9: NHP Subtype, n=653:

[0240] TCID-3153400, TCID-3749600, ABTB2, ACBD7, ACSL1, ACTA2, ADAMTS5, ADAMTS9, ADK, AGR2, AHNAK2, AHR, AIDA, AK1, AKR1C3, ALAS2, ALDH1A3, AMIGO2, AMOT, ANK2, ANO5, ANXA1, ANXA3, ANXA6, AOAH, AP3S1, APOO, AQP4, AQP9, ARHGAP24, ARL13B, ARL4A, ARMCX3, ARMCX6, ARNTL, ARSG, ASAP2, ATIC, ATP13A4, ATP6V0D2, B3GNT3, BCL9, BHLHE40, BHLHE41, BMP8A, BTBD11, BTG3, C10orf72, C11orf72, C11orf74, C11orf80, C12orf49, C16orf45, C19orf33, C1orf115, C1orf116, C2, C22orf9, C2orf40, C3, C4A, C4B, C4orf34, C5orf28, C6orf168, C6orf174, C7orf62, C8orf4, C8orf79, C9orf68, CA11, CADM1, CALCA, CAMK2N1, CAND1, CASC5, CAV1, CAV2, CCDC121, CCDC148, CCDC80, CCL13, CCND1, CCND1, CCND2, CD151, CD200, CD36, CDCP1, CDH11, CDH3, CDH6, CDK2, CDKL2, CDO1, CDON, CDR1, CEP55, CFB, CFH, CFHR1, CFI, CHAF1B, CHD4, CITED1, CKS2, CLC, CLDN1, CLDN10, CLDN16, CLDN4, CLDN7, CLEC4E, CLU, CNN3, COL1A1, COPZ2, CP, CPE, CRABP1, CRABP2, CSF3R, CST6, CTNNAL1, CTNNB1, CTSH, CTTN, CWH43, CXCL1, CXCL14, CXCL17, CXCL2, CXCL3, CXorf18, CXorf27, CYP24A1, CYP27A1, CYSLTR2, DAPK2, DCAF17, DCBLD2, DCUN1D3, DDAH1, DDB2, DDX52, DGKH, DGKI, DHRS1, DHRS3, DIO1, DIRAS3, DLC1, DLGAP5, DOCK9, DPP4, DPYSL3, DSG2, DSP, DST, DUOX1, DUOX2, DUOXA1, DUOXA2, DUSP4, DUSP5, DUSP6, DZIP1, ECE1, EDNRB, EGFR, EHBP1, EHD2, EHF, ELKS, ELMO1, EMP2, EMR3, ENAH, ENDOD1, EPB41, EPHA4, EPHX4, EPS8, ERBB3, ERI2, ERP27, ESRRG, ETNK2, ETV1, ETV5, F2RL2, FAAH2, FABP4, FAM111A, FAM111B, FAM164A, FAM176A, FAM20A, FAM84B, FAT4, FBXO2, FBXO21, FCN1, FCN2, FGF2, FGFR1OP2, FLJ20184, FLJ32810, FLJ42258, FLJ42258, FLRT3, FN1, FPR1, FPR2, FREM2, FRMD3, FXYD6, FZD4, FZD6, FZD7, G0S2, GABBR2, GABRB2, GADD45A, GALE, GALNT12, GALNT3, GALNT7, GBE1, GBP1, GBP3, GGCT, GLA, GLDN, GNG12, GOLT1A, GPR110, GPR110, GPR125, GPR98, GPRC5B, GRAMD3, GSN, GYPB, GYPC, GYPE, HEMGN, HEY2, HIST1H1A, HLA-DQB2, HMGA2, HMMR, HPN, HSD17B6, HSPH1, ICAM1, IGFBP5, IGFBP6, IGSF1, IKZF2, IL1RL1, IL2RA, IL8, IL8RA, IL8RB, IL8RB, IL8RBP, IL8RBP, IMPDH2, INPP5F, IPCEF1, IQGAP2, ITGA2, ITGA3, ITGA9, ITGB1, ITGB6, ITGB8, ITPR1, JUB, KAL1, KCNK5, KCNQ3, KCTD14, KDELC1, KDELR3, KHDRBS2, KIAA0284, KIAA0408, KIAA1217, KIF11, KIT, KLF8, KLK10, KLK7, KRT18, KRT19, LAMB3, LAMC1, LAMC2, LCA5, LCMT1, LCN2, LDOC1, LEMD1, LGALS3, LILRA1, LILRB1, LIMA1, LINGO2, LIPH, LMO3, LMO4, LOC100124692, LOC100127974, LOC100129112, LOC100129115,

LOC100129171, LOC100129961, LOC100130248, LOC100131102, LOC100131490, LOC100131938, LOC100131993, LOC100132338, LOC100132764, LOC283508, LOC440434, LOC554202, LOC643454, LOC648149, LOC653354, LOC653498, LOC730031, LONRF2, LOX, LPAR1, LPAR5, LPL, LRP1B, LRP2, LRRC69, LRRN1, LUM, LYRM1, MACC1, MAFG, MAMLD1, MAP2, MAPK6, MATN2, MBOAT2, MCM4, MCMI, MDK, ME1, MED13, MELK, MET, METTL7B, MEX3C, MFGE8, MGAM, MGAT1, MGAT4C, MGST1, MKI67, MLLT4, MMP16, MMP16, MNDA, MORC4, MPPED2, MPZL2, MRPL14, MT1F, MT1G, MT1H, MT1M, MT1P2, MT1P3, MTHFD1L, MUC1, MUC15, MVP, MXRA5, MYEF2, MYH10, MYO1B, MYO1D, MYO5A, MYO6, NAB2, NAE1, NAG20, NAV2, NCKAP1, NDC80, NDFIP2, NEDD4L, NELL2, NEXN, NFE2, NFIB, NIPAL3, NOD1, NPC2, NPEPPS, NPL, NPY1R, NRCAM, NRIP1, NRP2, NT5E, NUCB2, NUDT6, NUSAP1, OCIAD2, OCR1, ODZ1, ORAOV1, OSBPL1A, OSGEP, OSMR, P2RY13, P4HA2, PAM, PAPSS2, PARP4, PARVA, PBX1, PDE5A, PDE9A, PDGFRL, PDLIM1, PDLIM4, PDZRN4, PEG10, PERP, PGCP, PHEX, PHF16, PHLDB2, PHYHIP, PKHD1L1, PKP4, PLA2G16, PLA2G7, PLA2R1, PLAG1, PLAU, PLCD3, PLCL1, PLEKHA4, PLEKHA5, PLK2, PLS3, PLSCR4, PMEPA1, PON2, PPARGC1A, PPBP, PPL, PPP1R14C, PRCP, PRICKLE1, PRINS, PROK2, PROS1, PRR15, PRRG1, PRSS23, PSD3, PSD3, PTPN14, PTPRE, PTPRF, PTPRG, PTPRK, PTRF, QTRT1, RAB25, RAB27A, RAB32, RAB34, RAD23B, RAG2, RAI2, RAPGEF5, RARG, RASA1, RASD2, RBBP7, RBBP8, RBMS2, RCBTB2, RCE1, RDH5, RGS18, RGS2, RHOU, RND3, ROS1, RPL39L, RPRD1A, RPS6KA6, RRAS, RXRG, S100A12, S100A14, S100A16, S100A8, S100A9, SALL1, SAV1, SC4MOL, SCARA3, SCARNA11, SCEL, SCG5, SCNN1A, SCRN1, SDC4, SEH1L, SELL, SEMA3C, SEMA3D, SEPT11, SERINC2, SERPINA1, SERPINA2, SERPINE2, SERPING1, SFN, SFTPB, SGCB, SGCE, SGEF, SGMS2, SH2D4A, SH3PXD2A, SIRPA, SIRPB1, SLA, SLC12A2, SLC16A4, SLC16A6, SLC17A5, SLC24A5, SLC26A4, SLC26A7, SLC27A2, SLC27A6, SLC34A2, SLC35F2, SLC39A6, SLC4A4, SLC5A8, SLC7A11, SLC7A2, SLIT2, SLPI, SMOC2, SMURF2, SNCA, SNX1, SNX22, SNX7, SOAT1, SORBS2, SPATS2, SPATS2L, SPINT1, SPRED2, SPRY1, SPRY2, SRL, SSPN, ST3GAL5, STK32A, STXBP6, SULF1, SYNE1, SYT14, SYTL5, TACSTD2, TBC1D3F, TDRKH, TEAD1, TEAD1, TFCP2L1, TFF3, TFPI, TGFA, TGFB2, TGFBR1, TIMP1, TIPARP, TJP1, TJP2, TLCD1, TLR8, TM4SF1, TM4SF4, TM7SF4, TMEM100, TMEM117, TMEM133, TMEM163, TMEM171, TMEM215, TMEM90A, TMEM98, TMPRSS4, TNC, TNFRSF12A, TNFSF15, TOMM34, TPD52L1, TPO, TPX2, TRIP10, TRPC5, TSC22D1, TSPAN13, TSPAN6, TUBB1, TUBB6, TULP3, TUSC3, TXNRD1, TYMS, UCHL5, VNN1, VNN2, VNN3, WDR40A, WDR54, WIPI1, WNT5A, XKRX, XPR1, YIF1B, YTHDC2, ZBTB33, ZCCHC12, ZCCHC16, ZFP36L1, ZMAT3, ZMAT4, ZNF643, ZNF804B, ZYG11A.

[0241] (vii) List 10: MTC Subtype, n=48:

[0242] ANXA3, ATP13A4, BLNK, C10orf131, C6orf174, C8orf79, CALCA, CHGB, CP, CPE, DSG2, FREM2, GPR98, IGJ, IYD, KIAA0408, LOC100129171, LPCAT2, LRRC69, MACC1, MAPK6, MGAT4C, MGST1, MMP16, MT1G, MT1H, MT1M, MT1P2, MT1P3, MUC15, MYEF2, NT5E, PKHD1L1, PLS3, RBMS2, RIMS2, SCG3, SEMA3D, SLA, SLC24A5, SMOC2, SULF1, TOX, TSHZ2, TSPAN6, WDR72, ZFP36L1, ZNF208.

[0243] (viii) List 11: HC Subtype, n=65:

[0244] AIM2, APOBEC3F, APOBEC3G, ARHGAP19, BAGS, BCL2A1, BMP8A, C9orf68, CARD17, CARD8, CASP1, CD3D, CD96, CEP110, CLEC2B, CNN2, CPE, CYTH1, DENND4A, DNAJB14, DOCK8, DPYD, DUOX1, DUOX2, DYNC1I2, EGF, EPDR1, ETS1, GBP5, GIMAP2, GIMAP5, GIMAP7, GPR174, GZMK, HNRNPM, HSD17B6, IFI16, IFNAR2, IKZF3, IL7R, ITM2A, JAK2, KCNAB1, KHDRBS2, KLRC4, KLRG1, KLRK1, KYNU, LOC646358, MED13L, ND1, NFATC3, PAPSS2, PGCP, PTPRC, PYHIN1, SLIT1, SP140, SP140L, ST20, STAT4, TC2N, TLE4, ZEB2, ZNF143.

[0245] (ix) List 12: HA Subtype, n=24:

[0246] BCL2, CADM1, CAV1, CRABP1, CTNNB1, CYTH1, DIRAS3, IFITM1, IGFBP5, IGFBP6, LOX, MAP2, MATN2, MET, MKI67, MYO1B, ND1, NUCB2, SCG5, SCNN1A, SEL1L3, SGCE, TNFSF10, TRPC6.

[0247] (x) List 13: ATC Subtype, n=12:

[0248] CASC5, CEP55, COL12A1, DLGAP5, HMMR, KIF11, MELK, MKI67, NDC80, NUSAP1, PYGL, TPX2.

[0249] Dominant gene ontology of top 948 thyroid biomarkers are listed below:

[0250] List 14: Angiogenesis, n=23

[0251] ACTA2, ANXA2, ARHGAP24, CALCA, CAV1, CITED1, COL1A1, CXCL17, EGF, ELK3, IL8, LOX, PLCD3, PROK2, RASA1, SEMA3C, TCF7L2, TGFA, TGFB2, TIPARP, TNFRSF12A, ZFP36L1, ZFPM2.

[0252] List 15: Apoptosis, n=43

[0253] AHR, ANXA1, BAGS, BCL2, BCL2A1, BIRC5, C8orf4, CADM1, CD2, CLU, CTNNB1, DAPK2, DLC1, DNASE1L3, ECE1, ELMO1, FAM176A, FGF2, GADD45A, GULP1, GZMA, HIPK2, IL2RA, IL8RB, JAK2, NCKAP1, NOD1, NUPR1, PEG10, PERP, PROK2, RYR2, SLC5A8, STK17B, SULF1, TCF7L2, TGFB2, TNFAIP8, TNFRSF11B, TNFRSF12A, TNFSF10, VNN1, ZMAT3.

[0254] List 16: Cell Cycle, Transcription Factors, n=184

[0255] AEBP1, AHR, AK1, ANXA1, APOBEC3F, APOBEC3G, ARHGAP24, ARNTL, ATM, BCL2, BHLHE40, BHLHE41, BIRC5, BMP1, BMP8A, CADM1, CAND1, CARD8, CASP1, CCND1, CCND2, CDK2, CEP110, CEP55, CHAF1B, CHD4, CITED1, CKS2, CLU, CRABP2, CSGALNACT1, CTNNB1, CXCL1, CXCL17, DENND4A, DLGAP5, DST, DZIP1, EGF, EHF, EIF2B2, EIF4H, ELK3, EMP2, EPS8, ERBB2, ERBB3, ESRRG, ETS1, ETV1, ETV4, ETV5, FABP4, FGF2, G0S2, GADD45A, GLDN, GLIS3, GTF3A, HEMGN, HEY2, HIPK2, HLF, HMGA2, HPN, ID3, IFI16, IFNAR2, IGSF1, IKZF2, IKZF3, IKZF4, IL2RA, IL8, ITPR1, JAK2, JUB, KHDRBS2, KIF11, KLF8, KLK10, KRT18, LGALS3, LIFR, LMO3, LMO4, LRP2, LTBP2, LTBP3, MACC1, MAFG, MAMLD1, MAPK4, MAPK6, MCM4, MCMI, MDK, MED13, MED13L, MIS12, MKI67, MLLT3, MNDA, MTIF3, MYH10, NAB2, NAE1, NDC80, NFATC3, NFE2, NFIB, NFKBIZ, NOD1, NPAS3, NPAT, NRIP1, NRP2, NUDT6, NUPR1, NUSAP1, OSMR, PARD6B, PARP14, PARP4, PBX1, PDLIM1, PEG10, PIAS3, PLAG1, POU2F3, PPARGC1A, PPBP, PRMT6, PROK2, PTRF, PYHIN1, RARG, RBBP7, RBBP8, RGS2, RHOH, RRM2, RUNX1, RUNX2, RXRG, SALL1, SEMA3D, SERPINE2, SLIT1, SLIT2, SMAD9, SMURF2,

SP140, SPC25, SPOCK1, STAT4, SYNE1, TACSTD2, TCF7L2, TCFL5, TEAD1, TFCP2L1, TGFA, TGFB2, TGFBR1, TLE4, TNFAIP8, TNFRSF12A, TNFRSF17, TPX2, TSC22D1, TSHZ2, TULP3, TYMS, WNT5A, ZBTB33, ZCCHC12, ZEB2, ZFP36L1, ZFPM2, ZNF143, ZNF208, ZNF487, ZNF643.

[0256] List 17: Cell Membrane, n=410

[0257] ABCC3, ABCD2, ACSL1, ADAMTS5, ADAMTS9, ADORA1, AFAP1, AK1, ALOX5, AMIGO2, ANK2, ANO5, AP3S1, APOL1, APOO, AQP4, AQP9, ARMCX3, ARMCX6, ASAP2, ATP13A4, ATP6V0D2, ATP8A1, AVPR1A, B3GNT3, BCL2, BLNK, BTBD11, C10orf72, C17orf87, C1orf115, C4orf34, C5orf28, C6orf174, CADM1, CAMK2N1, CAV1, CAV2, CCDC109B, CD151, CD180, CD2, CD200, CD36, CD3D, CD48, CD48, CD52, CD69, CD79A, CD96, CDCP1, CDH11, CDH3, CDH6, CDON, CFB, CFI, CHI3L1, CLDN1, CLDN10, CLDN16, CLDN4, CLDN7, CLEC2B, CLEC4E, COL12A1, COL1A1, COPZ2, CP, CPE, CR2, CSF3R, CSGALNACT1, CTNNAL1, CTNNB1, CWH43, CYP1B1, CYP27A1, CYP4B1, CYSLTR1, CYSLTR2, CYTH1, DCAF17, DCBLD2, DHRS3, DIO1, DIRAS3, DLG2, DLG4, DNAJB14, DOCK9, DPP4, DPYSL3, DSG2, DUOX1, DUOX2, DUOXA1, DUOXA2, ECE1, EDNRB, EFEMP1, EGF, EGFR, EHBP1, EHD2, ELMO1, EMP2, EMR3, ENTPD1, EPB41, EPHA4, EPHX4, ERBB2, ERBB3, ERO1LB, F2RL2, F8, FAAH2, FAM176A, FAM84B, FAT4, FBLN5, FLRT3, FN1, FPR1, FPR2, FREM2, FRMD3, FXYD6, FZD4, FZD6, FZD7, GABBR2, GABRB2, GALNT12, GALNT3, GALNT7, GBP1, GBP3, GBP5, GIMAP2, GIMAP5, GJA4, GLDN, GNG12, GOLT1A, GPAM, GPR110, GPR125, GPR155, GPR174, GPR98, GPRC5B, GYPB, GYPC, GYPE, HIGD1A, HK1, HLA-DPB1, HNRNPM, HPN, HSD17B6, ICAM1, IFITM1, IFNAR2, IGSF1, IL1RAP, IL1RL1, IL2RA, IL7R, IL8RA, IL8RB, IPCEF1, ITGA2, ITGA3, ITGA4, ITGA9, ITGB1, ITGB4, ITGB6, ITGB8, ITM2A, ITPR1, IYD, JAK2, JUB, KAL1, KCNA3, KCNAB1, KCNK5, KCNQ3, KCTD14, KDELR3, KIAA1305, KIT, KLRB1, KLRC4, KLRG1, KLRK1, LAMB1, LAMC1, LEMD1, LGALS3, LIFR, LILRA1, LILRB1, LINGO2, LIPH, LPAR1, LPAR5, LPCAT2, LPL, LRP1B, LRP2, LRRN1, LRRN3, LUM, MATN2, MBOAT2, MET, MFGE8, MGAM, MGAT1, MGAT4C, MGST1, MMP16, MPZL2, MRC2, MUC1, MUC15, MYH10, MYO6, NAE1, NCAM1, NCKAP1, ND1, NDFIP2, NIPAL3, NPY1R, NRCAM, NRP2, NT5E, NUCB2, ODZ1, OSMR, P2RY13, PAM, PARD6B, PARP14, PARVA, PCDH1, PCNXL2, PERP, PHEX, PHLDB2, PIGN, PKHD1L1, PKP2, PLA2G16, PLA2R1, PLAU, PLCD3, PLEK, PLEKHA4, PLP2, PLSCR4, PLXNC1, PMEPA1, PON2, POR, PPAP2C, PPL, PPP1R14C, PRICKLE1, PRRG1, PSD3, PTK7, PTPRC, PTPRE, PTPRF, PTPRG, PTPRK, PTPRU, PTRF, RAB25, RAB27A, RARG, RASA1, RASD2, RCE1, RDH5, RGS13, RHOH, RHOU, RIMS2, RND3, ROS1, RRAS, RRAS2, RRBP1, RYR2, S100A12, SC4MOL, SCARA3, SCEL, SCNN1A, SDC4, SDK1, SEL1L3, SELL, SEMA3C, SEMA3D, SEMA4C, SERINC2, SERPINA1, SGCB, SGCE, SGMS2, SGPP2, SIRPA, SIRPB1, SLC12A2, SLC16A4, SLC16A6, SLC17A5, SLC24A5, SLC25A33, SLC26A4, SLC26A7, SLC27A2, SLC27A6, SLC34A2, SLC35D2, SLC35F2, SLC39A6, SLC4A4, SLC5A8, SLC7A11, SLC7A2, SMURF2, SNCA, SNX1, SOAT1, SPINT1, SPOCK1, SPRED2, SPRY1, SPRY2, SQLE, SSPN, ST3GAL5, STEAP2, STXBP6, SYNE1, SYT14, SYTL5, TACSTD2, TFCP2L1, TFF3, TFPI, TGFA, TGFB2, TGFBR1, TIMP1, TJP1, TJP2, TLCD1, TLR10, TLR8, TM4SF1, TM4SF4, TM7SF4, TMEM100, TMEM117, TMEM133, TMEM156, TMEM163, TMEM171, TMEM215, TMEM220, TMEM90A, TMEM98, TMPRSS4, TNC, TNFRSF11B, TNFRSF12A, TNFRSF17, TNFSF10, TNFSF15, TOMM34, TPO, TRIP10, TRPC5, TRPC6, TSPAN13, TSPAN6, TSPAN8, TULP3, TUSC3, VAMP1, VNN1, VNN2, VNN3, WNT5A, XKRX, XPR1, YIF1B, YIPF1, ZBTB33.

[0258] List 18: Rare Membrane Components, n=55

[0259] AMOT, ANXA1, ANXA2, CALCA, CAMK2N1, CAV1, CAV2, CCDC80, CLU, CST6, CTNNB1, CTTN, DLC1, DPP4, DSG2, DSP, DST, ENAH, GJA4, HIPK2, ITGB1, ITGB4, JAK2, JUB, KRT19, LCP1, LRP2, MYH10, MYO5A, MYO6, NEB, PARVA, PCDH1, PERP, PKP2, PKP4, PLEK, PPL, PTRF, RAB34, RASA1, RYR2, SCEL, SGCB, SGCE, SLC27A6, SLIT1, SPRY1, SRL, SSPN, SYNE1, TGFB2, TIAM2, TJP1, TNFRSF12A.

[0260] List 19: Cell-Cell Adhesion, n=85

[0261] AEBP1, AFAP1, AMIGO2, ARHGAP24, BCL2, CADM1, CALCA, CD151, CD2, CD36, CD96, CDH3, CDH6, CDON, CLDN1, CLDN10, COL12A1, CSF3R, CTNNAL1, CTNNB1, DCBLD2, DLC1, DSG2, DST, EGFR, ENAH, ENTPD1, EPDR1, F8, FAT4, FBLN5, FLRT3, FN1, FPR2, FREM2, GPR98, ICAM1, IGFBP7, IL1RL1, ITGA2, ITGA3, ITGA4, ITGA9, ITGB1, ITGB4, ITGB6, ITGB8, JUB, KAL1, LAMB1, LAMB3, LAMC1, LAMC2, LIMA1, MFGE8, MLLT4, MPZL2, NCAM1, NELL2, NRCAM, NRP2, PARVA, PCDH1, PERP, PKP2, PKP4, PLXNC1, PTK7, PTPRC, PTPRF, PTPRK, PTPRU, RHOU, RND3, SDK1, SELL, SGCE, SIRPA, SPOCK1, SPP1, SSPN, TJP1, TNC, TNFRSF12A, VNN1.

[0262] List 20: Apical Cell Membrane, n=15

[0263] ANK2, ATP6V0D2, CTNNB1, CTNNB1, DPP4, DUOX1, ERBB2, ERBB3, F2RL2, FZD6, LRP2, SCNN1A, SLC26A4, SLC34A2, TFF3.

[0264] List 21: Basolateral, Lateral Cell Membrane, n=28

[0265] ANK2, ANXA1, ANXA2, CADM1, CCDC80, CTNNB1, CTTN, DSP, DST, EGFR, EPB41, ERBB2, ERBB3, FREM2, LAMB1, LAMB3, LAMC1, LAMC2, MET, MYH10, MYO6, PTPRK, SLC26A7, SMOC2, SNCA, TIMP3, TJP1, TRIP10.

[0266] List 22: Integrins, n=14

[0267] ADAMTS5, DST, FBLN5, ICAM1, ITGA2, ITGA3, ITGA4, ITGA9, ITGB1, ITGB4, ITGB6, ITGB8, MFGE8, PLEK.

[0268] List 23: Cell Junction, n=40

[0269] AMOT, ARHGAP24, ARHGAP24, CADM1, CAMK2N1, CLDN1, CLDN10, CLDN16, CLDN4, CLDN7, CNN2, DLG2, DLG4, DPYSL3, DSP, ENAH, GABBR2, GABRB2, GJA4, JUB, LIMA1, MLLT4, NCKAP1, NEXN, PARD6B, PARVA, PCDH1, PERP, PPL, PSD3, PTPRK, PTPRU, RHOU, RIMS2, SH3PXD2A, SSPN, TGFB2, TJP1, TJP2, VAMP1.

[0270] List 24: Cell Surface, n=17

[0271] CD36, DCBLD2, DPP4, GPR98, HMMR, IL1RL1, IL8RB, ITGA4, ITGB1, KAL1, MMP16, PTPRK, SDC4, SULF1, TGFA, TM7SF4, TNFRSF12A.

[0272] List 25: Extracellular Space, n=156

[0273] ADAMTS5, ADAMTS9, AEBP1, AGR2, ANGPTL1, ANXA2, APOL1, APOO, BMP1, BMP8A, C12orf49, C2, C2orf40, C3, C4A, C4B, C4orf7, CA11,

CALCA, CCDC80, CCL13, CCL19, CDCP1, CFB, CFH, CFHR1, CFI, CHGB, CHI3L1, CLU, COL12A1, COL1A1, CP, CPE, CSF3R, CST6, CXCL1, CXCL11, CXCL13, CXCL14, CXCL17, CXCL2, CXCL3, CXCL9, DPP4, EFEMP1, EGF, EGFR, EMR3, ENDOD1, EPDR1, ERBB3, F8, FAM20A, FAM55C, FBLN5, FCN1, FCN2, FGF2, FIBIN, FN1, FXYD6, GLA, GSN, GZMA, GZMK, ICAM1, IFNAR2, IGFBP5, IGFBP6, IGFBP7, IGJ, IGKC, IGKV1-5, IGKV3-20, IGKV3D-11, IGSF1, IL1RAP, IL1RL1, IL7R, IL8, KAL1, KIT, KLK10, KLK7, LAMB1, LAMB3, LAMC1, LAMC2, LCN2, LIFR, LIPH, LOC652694, LOX, LPL, LTBP2, LTBP3, LUM, LYZ, MATN2, MDK, MFGE8, MMP16, MUC1, MUC15, MXRA5, NCAM1, NELL2, NPC2, NUCB2, ODZ1, PAM, PDGFRL, PGCP, PLA2G7, PLA2R1, PLAU, PON2, PPBP, PROK2, PROS1, PRRG1, PRSS23, PXDNL, RNASE1, RNASET2, SCG3, SCG5, SEMA3C, SEMA3D, SEPP1, SERPINA1, SERPINE2, SERPING1, SFN, SFTPB, SLIT1, SLIT2, SLPI, SMOC2, SPINT1, SPOCK1, SPP1, SULF1, TFF3, TFPI, TGFA, TGFB2, THSD4, TIMP1, TIMP3, TNC, TNFRSF11B, TNFSF10, TNFSF15, WNT5A.

[0274] List 26: Cytoskeleton, n=94

[0275] ACTA2, ADORA1, AFAP1, AMOT, ANK2, ANXA2, AP3S1, ARHGAP24, ATM, ATP8A1, BCL2, BIRC5, C2orf40, CASC5, CLU, CNN2, CNN3, COL12A1, COL1A1, COPZ2, CTNNAL1, CTNNB1, CTTN, CXCL1, DLG4, DLGAP5, DPYSL3, DST, DYNC1I2, DYNLT1, EGFR, ELMO1, ENAH, EPB41, EPS8, FAM82B, FRMD3, GPRC5B, GSN, GYPC, IGF2BP2, IQGAP2, JAK2, JUB, KATNAL2, KIAA0284, KIF11, KRT18, LCA5, LCP1, LIMA1, LOX, LUM, MAP2, MPZL2, MYH10, MYO1B, MYO1D, MYO5A, MYO6, NEB, NEXN, NFE2, NUSAP1, PARVA, PDLIM1, PKP2, PLEK, PLS3, PPL, PTPN14, RHOU, RND3, S100A9, SCNN1A, SDC4, SGCB, SGCE, SNCA, SORBS2, SPRED2, SPRY2, STK17B, SYNE1, TGFB2, TGFBR1, TMSB10, TMSB15A, TPX2, TRIP10, TUBB1, TUBB6, VAMP1, WIPI1.

[0276] In some embodiments, the present invention provides a method of classifying cancer comprising the steps of: obtaining a biological sample comprising gene expression products; determining the expression level for one or more gene expression products of the biological sample; and identifying the biological sample as cancerous wherein the gene expression level is indicative of the presence of thyroid cancer in the biological sample. This can be done by correlating the gene expression levels with the presence of thyroid cancer in the biological sample. In one embodiment, the gene expression products are selected from one or more genes listed in Table 2. In some embodiments, the method further includes identifying the biological sample as positive for a cancer that has metastasized to thyroid from a non-thyroid organ if there is a difference in the gene expression levels between the biological sample and a control sample at a specified confidence level.

[0277] Biomarkers involved in metastasis to thyroid from a non-thyroid organ are provided. Such metastatic cancers that metastasize to thyroid and can be diagnosed using the subject methods of the present invention include but are not limited to metastatic parathyroid cancer, metastatic melanoma, metastatic renal carcinoma, metastatic breast carcinoma, and metastatic B cell lymphoma. Exemplary biomarkers that can be used by the subject methods to diagnose metastasis to thyroid are listed in Table 2.

TABLE 2

Biomarkers involved in metastasis to thyroid

Type of metastasis	Number of genes	Genes
Top Biomarkers of Non-thyroid Metastases to the Thyroid	73	ACADL, ATP13A4, BIRC5, BTG3, C2orf40, C7orf62, CD24, CHEK1, CP, CRABP1, CXADR, CXADRP2, DIO1, DIO2, EPCAM, EPR1, GPX3, HSD17B6, IQCA1, IYD, KCNJ15, KCNJ16, KRT7, LMO3, LOC100129258, LOC100130518, LPCAT2, LRRC2, LRRC69, MAL2, MAPK6, MGAT4C, MGC9913, MT1F, MT1G, MT1H, MT1P2, MUC15, NEBL, NPNT, NTRK2, PAR1, PCP4, PDE1A, PDE8B, PKHD1L1, PLS3, PVRL2, PVRL3, RGN, RPL3, RRM2, SCD, SEMA3D, SH3BGRL2, SLC26A4, SLC26A7, SNRPN, SPC25, SYT14, TBCKL, TCEAL2, TCEAL4, TG, TPO, TSHR, WDR72, ZBED2, ZNF208, ZNF43, ZNF676, ZNF728, ZNF99
Parathyroid Metastasis to Thyroid	101	TCID-2688277, ACSL3, ACTR3B, ADAM23, ADH5, ARP11, AS3MT, BANK1, C10orf32, C11orf41, C2orf67, C7orf62, C8orf34, CA8, CASR, CD109, CD226, CD24, CD44, CDCA7L, CHEK1, CLDN1, CP, DIO2, DMRT2, DNAH11, DPP4, ELOVL2, ENPEP, EPHA7, ESRRG, EYA1, FMN2, GCM2, GPR160, GPR64, HSD17B6, ID2, ED2B, IYD, KIDINS220, KIF13B, KL, LGI2, LMO3, LOC100131599, LOC150786, LPL, LRRC69, MAPK6, MGST1, MT1F, MT1G, MT1H, MT1P2, MUC15, NAALADL2, NPNT, OGN, PDE8B, PEX5L, PKHD1L1, PLA2G4A, PLCB1, PRLR, PTH, PTN, PTPRD, PTTG1, PTTG2, PVALB, PVRL2, RAB6A, RAB6C, RAPGEF5, RARRES2, RGN, RNF217, RPE, SACS, SEMA3D, SGK1, SLA, SLC15A1, SLC26A4, SLC26A7, SLC7A8, SPOCK3, ST3GAL5, STXBP5, SYCP2L, TBCKL, TG, TINF2, TMEM167A, TPO, TSHR, TTR, WDR72, YAP1, ZBED2
Melanoma Metastasis to Thyroid	190	TCID-2840750, ABCB5, AHNAK2, ALX1, ANLN, AP1S2, APOD, ASB11, ATP13A4, ATP1B1, ATRNL1, AZGP1, BACE2, BAMBI, BCHE, BIRC5, BRIP1, BZW1, BZW1L1, C2orf40, C6orf218, C7orf62, CA14, CASC1, CCNB2, CD24,

TABLE 2-continued

Biomarkers involved in metastasis to thyroid

Type of metastasis	Number of genes	Genes
		CDH19, CDK2, CDKN3, CENPF, CHRNA5, CP, CRABP1, DCT, DEPDC1, DIO1, DIO2, DLGAP5, DSCC1, DSP, EDNRB, EIF1AY, EIF4A1, ENPP1, EPCAM, EPR1, ESRP1, FABP7, FANCI, GAS2L3, GGH, GPM6B, GPNMB, GPR19, GPX3, GULP1, GYG2, HAS2, HEATR5A, HMCN1, HTN1, IL13RA2, IQCA1, IYD, KCNJ15, KCNJ16, KIAA0894, KIF23, KRT7, KRTAP19-1, LGALS1, LMO3, LOC100129171, LOC100129258, LOC100130275, LOC100130357, LOC100130518, LOC100131821, LOC145694, LOC653653, LRP2, LRRC69, LSAMP, LUM, MAL2, MAPK6, MGC87042, MITF, MLANA, MME, MND1, MOXD1, MSMB, MUC15, NDC80, NEBL, NLGN1, NOX4, NPNT, NTRK2, NUDT10, NUDT11, PAX3, PBK, PCP4, PDE3B, PDE8B, PI15, PICA, PIR, PKHD1L1, PLP1, PLXNC1, POLG, POMGNT1, POPDC3, POSTN, PRAME, PRAMEL, PTPRZ1, PVRL2, PYGL, QPCT, RGN, RNF128, ROPN1, ROPN1B, RPL3, RPSA, RPSAP15, RPSAP58, S100B, SACS, SAMD12, SCD, SEMA3C, SERPINA3, SERPINE2, SERPINF1, SHC4, SILV, SLA, SLC16A1, SLC26A4, SLC26A7, SLC39A6, SLC45A2, SLC5A8, SLC6A15, SNAI2, SNCA, SNORA48, SNORA67, SORBS1, SPC25, SPP1, SPRY2, SRPX, ST3GAL6, STEAP1, STK33, TBC1D7, TBCKL, TCEAL2, TCEAL4, TCN1, TF, TFAP2A, TG, TMP2, TMSB15A, TMSB15B, TNFRSF11B, TOP2A, TPO, TPX2, TRPM1, TSHR, TSPAN1, TUBB4, TYR, TYRL, TYRP1, WDR72, ZBED2, ZNF208, ZNF43, ZNF676, ZNF728, ZNF99
Renal Carcinoma Metastasis to Thyroid	130	TCID-2763154, ADFP, AKR1C3, ALPK2, APOL1, ASPA, ATP13A4, ATP8A1, BHMT, BHMT2, BICC1, BIRC3, C12orf75, C1S, C2orf40, C3, C7orf62, CA12, CDH6, CLRN3, CP, CYB5A, DAB2, DEFB1, DIO2, EFNA5, EGLN3, EIF1AY, ENPEP, ENPP1, ENPP3, EPCAM, ESRP1, FABP6, FABP7, FAM133B, FCGR3A, FCGR3B, FXYD2, GAS2L3, GLYAT, GSTA1, GSTA2, GSTA5, HAVCR1, HLA-DQA1, HPS3, IGFBP3, IL20RB, IYD, KMO, LEPREL1, LMO3, LOC100101266, LOC100129233, LOC100129518, LOC100130232, LOC100130518, LOC100133763, LOC728640, LOX, LRRC69, MAPK6, MGC9913, MME, MMP7, MT1G, MUC15, NEBL, NLGN1, NNMT, NPNT, NR1H4, OPN3, OSMR, PCOLCE2, PCP4, PDE8B, PDZK1IP1, PIGA, PKHD1L1, POSTN, PREPL, PTHLH, RPS6KA6, S100A10, SAA1, SAA2, SCD, SLC16A1, SLC16A4, SLC17A3, SLC26A4, SLC26A7, SLC3A1, SLCO4C1, SNX10, SOD2, SPINK1, SPP1, SYT14, TBCKL, TCEAL2, TCEAL4, TG, TMEM161B, TMEM176A, TMEM45A, TNFAIP6, TNFSF10, TPO, TSHR, UGT1A1, UGT1A10, UGT1A3, UGT1A4, UGT1A5, UGT1A6, UGT1A7, UGT1A8, UGT1A9, UGT2A3, UGT2B7, VCAM1, VCAN, ZNF208, ZNF43, ZNF676, ZNF728, ZNF99
Breast Carcinoma Metastasis to Thyroid	117	TCID-3777770, ACADL, AGR2, AGR3, ALDH1A1, ANLN, ASPM, ATP13A4, AZGP1, BIRC5, BRIP1, C10orf81, C7orf62, C8orf79, CA2, CCNB2, CCNE2, CDC2, CDC6, CDKN3, CENPF, CHEK1, CP, CSNK1G1, DEPDC1, DIO1, DIO2, DLGAP5, DTL, EHF, EPR1, EZH2, FAM111B, FANCI, GALNT5, GPX3, HHEX, HPS3, IQCA1, ITGB3, IYD, KCNJ15, KCNJ16, KIAA0101, KIF23, LMO3, LOC100129258, LOC100130518, LOC100131821, LOC145694, LRP2, LRRC2, LRRC69, MAPK6, MELK, MGAT4C, MKI67, MND1, MUC15, MYB, NDC80, NPY1R, NUF2, NUSAP1, PAR1, PARP8, PBK, PCP4, PDE1A, PDE8B, PI15, PIP, PKHD1L1, POLG, PPARGC1A, PRC1, PVRL2, PVRL3, RAD51AP1, RGN, RPL3, RRM2, SAA1, SAA2, SCD, SCGB1D2, SCGB2A2, SEMA3C, SERPINA3, SLA, SLC26A4, SLC26A7, SNRPN, SPC25, ST3GAL5, STK33, SULT1C2, SYCP2, SYT14, TFF1, TG, THBS1, TOP2A, TPO, TPX2, TRPS1, TSHR, TTK, UNQ353, VTCN1, WDR72, ZBED2, ZNF208, ZNF43, ZNF676, ZNF728, ZNF99
B cell Lymphoma Metastasis to Thyroid	160	ACADL, AIM2, ALDH1A1, ALG9, APP, ARHGAP29, ATP13A4, ATP1B1, BCL2A1, BIRC3, BIRC5, BTG3, C11orf74, C2orf40, C7orf62, CALCRL, CALD1, CD180, CD24, CD48, CD52, CD53, CDH1, CNN3, COX11, CP, CPE,

TABLE 2-continued

Biomarkers involved in metastasis to thyroid		
Type of metastasis	Number of genes	Genes
		CR2, CRYAB, CXADR, CXADRP2, CXorf65, DCBLD2, DIO2, DLGAP5, DSP, EAF2, EFCAB2, ENPP1, EPCAM, EPR1, ESRP1, FABP4, FDXACB1, FNBP1L, GJA1, GNAI1, GNG12, GPR174, GPX3, GTSF1, HCG11, IKZF3, IL2RG, IQCA1, IYD, KCNJ16, KLHL6, LAPTM5, LCP1, LIFR, LMO3, LOC100128219, LOC100129258, LOC100130518, LOC100131821, LOC100131938, LOC647979, LOC729828, LPCAT2, LPHN2, LRIG3, LRMP, LRP2, LRRC6, LRRC69, MAL2, MAOA, MAPK6, MATN2, MCOLN2, MGC9913, MGP, MKI67, MS4A1, MT1F, MT1G, MT1H, MT1L, MT1P2, MUC15, NCKAP1, NCKAP1L, NEBL, NME5, NPNT, NUDT12, PAR1, PBX1, PCP4, PDE8B, PDK4, PERP, PFN2, PKHD1L1, PLOD2, PLS3, POMGNT1, PPARGC1A, PPIC, PTPRC, PTPRM, PVRL3, RASEF, RGN, RGS13, RGS5, RHOH, RPL3, RPL37AP8, RRM2, S100A1, S100A13, SDC2, SELL, SEMA3D, SH3BGRL2, SLC26A4, SLC26A7, SMARCA1, SNRPN, SP140, SP140L, SPARCL1, SPC25, SPTLC3, ST20, STK17B, SYT14, TBCKL, TCEAL2, TCEAL4, TEAD1, TG, TJP1, TLR10, TOM1L1, TOP2A, TSHR, TSPAN1, TSPAN6, UACA, VNN2, WBP5, WDR72, ZNF208, ZNF43, ZNF676, ZNF728, ZNF99

[0278] (viii) Classification Error Rates

[0279] In some embodiments, top thyroid biomarkers (948 genes) are subdivided into bins (50 TCIDs per bin) to demonstrate the minimum number of genes required to achieve an overall classification error rate of less than 4% (FIG. **1**). The original TCIDs used for classification correspond to the Affymetrix Human Exon 1.0ST microarray chip and each may map to more than one gene or no genes at all (Affymetrix annotation file: HuEx-1_0-st-v2.na29.hg18.transcript.csv). When no genes map to a TCID the biomarker is denoted as TCID-######.

[0280] List 27: Error Rate Bin 1 (TCID 1-50 (n=50), Gene Symbols, n=58)

[0281] AMIGO2, C11orf72, C11orf80, C6orf174, CAMK2N1, CDH3, CITED1, CLDN1, CLDN16, CST6, CXorf27, DLC1, EMP2, ERBB3, FZD4, GABRB2, GOLT1A, HEY2, HMGA2, IGFBP6, ITGA2, KCNQ3, KIAA0408, KRT19, LIPH, LOC100129115, MACC1, MDK, MET, METTL7B, MFGE8, MPZL2, NAB2, NOD1, NRCAM, PDE5A, PDLIM4, PHYHIP, PLAG1, PLCD3, PRICKLE1, PROS1, PRR15, PRSS23, PTPRF, QTRT1, RCE1, RDH5, ROS1, RXRG, SDC4, SLC27A6, SLC34A2, SYTL5, TNFRSF12A, TRPC5, TUSC3, ZCCHC12.

[0282] List 28: Error Rate Bin 2 (TCID 51-100 (n=50), Gene Symbols, n=59)

[0283] AHNAK2, AIDA, AMOT, ARMCX3, BCL9, C1orf115, C1orf116, C4A, C4B, C6orf168, CCDC121, CCND1, CDH6, CFI, CLDN10, CLU, CRABP2, CXCL14, DOCK9, DZIP1, EDNRB, EHD2, ENDOD1, EPHA4, EPS8, ETNK2, FAM176A, FLJ42258, HPN, ITGA3, ITGB8, KCNK5, KLK10, LAMB3, LEMD1, LOC100129112, LOC100132338, LOC554202, MAFG, MAMLD1, MED13, MYH10, NELL2, PCNXL2, PDE9A, PLEKHA4, RAB34, RARG, SCG5, SFTPB, SLC35F2, SLIT2, TACSTD2, TGFA, TIMP1, TMEM100, TMPRSS4, TNC, ZCCHC16.

[0284] List 29: Error Rate Bin 3 (TCID 101-150 (n=50), Gene Symbols, n=52)

[0285] ABTB2, ADAMTS9, ADORA1, B3GNT3, BMP1, C19orf33, C3, CDH11, CLIP3, COL1A1, CXCL17, CYSLTR2, DAPK2, DHRS3, DIRAS3, DPYSL3, DUSP4, ECE1, FBXO2, FGF2, FN1, GALE, GPRC5B, GSN, IKZF4, IQGAP2, ITGB4, KIAA0284, KLF8, KLK7, LONRF2, LPAR5, MPPED2, MUC1, NRIP1, NUDT6, ODZ1, PAM, POU2F3, PPL, PTRF, RAPGEF5, RASD2, SCARA3, SCEL, SEMA4C, SNX22, SPRY1, SSPN, TM4SF4, XPR1, YIF1B.

[0286] List 30: Error Rate Bin 4 (TCID 151-200 (n=50), Gene Symbols, n=58)

[0287] AFAP1, ARMCX6, ARNTL, ASAP2, C2, C8orf4, CCDC148, CFB, CHAF1B, CLDN4, DLG4, DUSP6, ELMO1, FAAH2, FAM20A, FLRT3, FRMD3, GALNT12, GALNT7, IGFBP5, IKZF2, ISYNA1, LOC100131490, LOC648149, LOC653354, LRP1B, MAP2, MRC2, MT1F, MT1G, MT1H, MT1P2, MYEF2, NPAS3, PARD6B, PCDH1, PMEPA1, PPAP2C, PSD3, PTPRK, PTPRU, RAI2, RRAS, SDK1, SERPINA1, SERPINA2, SGMS2, SLC24A5, SMURF2, SPATS2L, SPINT1, TDRKH, TIPARP, TM4SF1, TMEM98, WNT5A, XKRX, ZMAT4.

[0288] List 31: Error Rate Bin 5 (TCID 201-250 (n=50), Gene Symbols, n=53)

[0289] ABCC3, AEBP1, C16orf45, C19orf33, CA11, CCND2, CDO1, CYP4B1, DOK4, DUSP5, ETV4, FAM111A, FN1, GABBR2, GGCT, GJA4, GPR110, HIPK2, ITGA9, JUB, KDELR3, KIAA1217, LAMC2, LCA5, LTBP2, LTBP3, MAPK6, NAV2, NIPAL3, OSMR, PDZRN4, PHLDB2, PIAS3, PKHD1L1, PKP2, PKP4, PRINS, PTK7, PTPRG, RAB27A, RAD23B, RASA1, RICH2, SCRN1, SFN, ST3GAL5, STK32A, TCERG1L, THSD4, TJP2, TM7SF4, TPO, YIF1B.

IX. Compositions

[0290] (i) Gene Expression Products and Splice Variants of the Present Invention

[0291] Molecular profiling may also include but is not limited to assays of the present disclosure including assays for one or more of the following: proteins, protein expression products, DNA, DNA polymorphisms, RNA, RNA expression products, RNA expression product levels, or RNA expression product splice variants of the genes provided in FIG. **2-6**, **9-13**, **16** or **17**. In some cases, the methods of the present invention provide for improved cancer diagnostics by molecular profiling of about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 120, 140, 160, 180, 200, 240, 280, 300, 350, 400, 450, 500, 600, 700, 800, 1000, 1500, 2000, 2500, 3000, 3500, 4000, 5000 or more DNA polymorphisms, expression product markers, and/or alternative splice variant markers.

[0292] In one embodiment, molecular profiling involves microarray hybridization that is performed to determine gene expression product levels for one or more genes selected from: FIG. **2-6**, **9-13**, **16** or **17**. In some cases, gene expression product levels of one or more genes from one group are compared to gene expression product levels of one or more genes in another group or groups. As an example only and without limitation, the expression level of gene TPO may be compared to the expression level of gene GAPDH. In another embodiment, gene expression levels are determined for one or more genes involved in one or more of the following metabolic or signaling pathways: thyroid hormone production and/or release, protein kinase signaling pathways, lipid kinase signaling pathways, and cyclins. In some cases, the methods of the present invention provide for analysis of gene expression product levels and or alternative exon usage of at least one gene of 1, 2, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 14, or 15 or more different metabolic or signaling pathways.

[0293] (ii) Compositions of the Present Invention

[0294] Compositions of the present disclosure are also provided which composition comprises one or more of the following: nucleotides (e.g. DNA or RNA) corresponding to the genes or a portion of the genes provided in FIG. **2-6**, **9-13**, **16** or **17**, and nucleotides (e.g. DNA or RNA) corresponding to the complement of the genes or a portion of the complement of the genes provided in FIG. **2-6**, **9-13**, **16** or **17**. The nucleotides of the present invention can be at least about 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 100, 150, 200, 250, 300, 350, or about 400 or 500 nucleotides in length. In some embodiments of the present invention, the nucleotides can be natural or man-made derivatives of ribonucleic acid or deoxyribonucleic acid including but not limited to peptide nucleic acids, pyranosyl RNA, nucleosides, methylated nucleic acid, pegylated nucleic acid, cyclic nucleotides, and chemically modified nucleotides. In some of the compositions of the present invention, nucleotides of the present invention have been chemically modified to include a detectable label. In some embodiments of the present invention the biological sample has been chemically modified to include a label.

[0295] A further composition of the present disclosure comprises oligonucleotides for detecting (i.e. measuring) the expression products of the genes provided in FIG. **2-6**, **9-13**, **16** or **17** and their complement. A further composition of the present disclosure comprises oligonucleotides for detecting (i.e. measuring) the expression products of polymorphic alleles of the genes provided in FIG. **2-6**, **9-13**, **16** or **17** and their complement. Such polymorphic alleles include but are not limited to splice site variants, single nucleotide polymorphisms, variable number repeat polymorphisms, insertions, deletions, and homologues. In some cases, the variant alleles are between about 99.9% and about 70% identical to the genes listed in FIG. **6**, including about 99.75%, 99.5%, 99.25%, 99%, 97.5%, 95%, 92.5%, 90%, 85%, 80%, 75%, and about 70% identical. In some cases, the variant alleles differ by between about 1 nucleotide and about 500 nucleotides from the genes provided in FIG. **2-6**, **9-13**, **16** or **17**, including about 1, 2, 3, 5, 7, 10, 15, 20, 25, 30, 35, 50, 75, 100, 150, 200, 250, 300, and about 400 nucleotides.

[0296] In some embodiments, the composition of the present invention may be specifically selected from the top differentially expressed gene products between benign and malignant samples, or the top differentially spliced gene products between benign and malignant samples, or the top differentially expressed gene products between normal and benign or malignant samples, or the top differentially spliced gene products between normal and benign or malignant samples. In some cases the top differentially expressed gene products may be selected from FIG. **2** and/or FIG. **4**. In some cases, the top differentially spliced gene products may be selected from FIG. **3** and/or FIG. **5**.

IX. Business Methods

[0297] As described herein, the term customer or potential customer refers to individuals or entities that may utilize methods or services of the molecular profiling business. Potential customers for the molecular profiling methods and services described herein include for example, patients, subjects, physicians, cytological labs, health care providers, researchers, insurance companies, government entities such as Medicaid, employers, or any other entity interested in achieving more economical or effective system for diagnosing, monitoring and treating cancer.

[0298] Such parties can utilize the molecular profiling results, for example, to selectively indicate expensive drugs or therapeutic interventions to patients likely to benefit the most from said drugs or interventions, or to identify individuals who would not benefit or may be harmed by the unnecessary use of drugs or other therapeutic interventions.

[0299] (i) Methods of Marketing

[0300] The services of the molecular profiling business of the present invention may be marketed to individuals concerned about their health, physicians or other medical professionals, for example as a method of enhancing diagnosis and care; cytological labs, for example as a service for providing enhanced diagnosis to a client; health care providers, insurance companies, and government entities, for example as a method for reducing costs by eliminating unwarranted therapeutic interventions. Methods of marketing to potential clients, further includes marketing of database access for researchers and physicians seeking to find new correlations between gene expression products and diseases or conditions.

[0301] The methods of marketing may include the use of print, radio, television, or internet based advertisement to potential customers. Potential customers may be marketed to through specific media, for example, endocrinologists may be marketed to by placing advertisements in trade magazines and medical journals including but not limited to *The Journal of the American Medical Association, Physicians*

Practice, American Medical News, Consultant, Medical Economics, Physician's Money Digest, American Family Physician, Monthly Prescribing Reference, Physicians' Travel and Meeting Guide, Patient Care, Cortlandt Forum, Internal Medicine News, Hospital Physician, Family Practice Management, Internal Medicine World Report, Women's Health in Primary Care, Family Practice News, Physician's Weekly, Health Monitor, The Endocrinologist, Journal of Endocrinology, The Open Endocrinology Journal, and *The Journal of Molecular Endocrinology*. Marketing may also take the form of collaborating with a medical professional to perform experiments using the methods and services of the present invention and in some cases publish the results or seek funding for further research. In some cases, methods of marketing may include the use of physician or medical professional databases such as, for example, the American Medical Association (AMA) database, to determine contact information.

[0302] In one embodiment methods of marketing comprises collaborating with cytological testing laboratories to offer a molecular profiling service to customers whose samples cannot be unambiguously diagnosed using routine methods.

[0303] (ii) Business Methods Utilizing a Computer

[0304] The molecular profiling business may utilize one or more computers in the methods of the present invention such as a computer **800** as illustrated in FIG. **22**. The computer **800** may be used for managing customer and sample information such as sample or customer tracking, database management, analyzing molecular profiling data, analyzing cytological data, storing data, billing, marketing, reporting results, or storing results. The computer may include a monitor **807** or other graphical interface for displaying data, results, billing information, marketing information (e.g. demographics), customer information, or sample information. The computer may also include means for data or information input **816**, **815**. The computer may include a processing unit **801** and fixed **803** or removable **811** media or a combination thereof. The computer may be accessed by a user in physical proximity to the computer, for example via a keyboard and/or mouse, or by a user **822** that does not necessarily have access to the physical computer through a communication medium **805** such as a modem, an internet connection, a telephone connection, or a wired or wireless communication signal carrier wave. In some cases, the computer may be connected to a server **809** or other communication device for relaying information from a user to the computer or from the computer to a user. In some cases, the user may store data or information obtained from the computer through a communication medium **805** on media, such as removable media **812**. It is envisioned that data relating to the present invention can be transmitted over such networks or connections for reception and/or review by a party. The receiving party can be but is not limited to an individual, a health care provider or a health care manager. In one embodiment, a computer-readable medium includes a medium suitable for transmission of a result of an analysis of a biological sample, such as exosome bio-signatures. The medium can include a result regarding an exosome biosignature of a subject, wherein such a result is derived using the methods described herein.

[0305] The molecular profiling business may enter sample information into a database for the purpose of one or more of the following: inventory tracking, assay result tracking, order tracking, customer management, customer service, billing, and sales. Sample information may include, but is not limited to: customer name, unique customer identification, customer associated medical professional, indicated assay or assays, assay results, adequacy status, indicated adequacy tests, medical history of the individual, preliminary diagnosis, suspected diagnosis, sample history, insurance provider, medical provider, third party testing center or any information suitable for storage in a database. Sample history may include but is not limited to: age of the sample, type of sample, method of acquisition, method of storage, or method of transport.

[0306] The database may be accessible by a customer, medical professional, insurance provider, third party, or any individual or entity which the molecular profiling business grants access. Database access may take the form of electronic communication such as a computer or telephone. The database may be accessed through an intermediary such as a customer service representative, business representative, consultant, independent testing center, or medical professional. The availability or degree of database access or sample information, such as assay results, may change upon payment of a fee for products and services rendered or to be rendered. The degree of database access or sample information may be restricted to comply with generally accepted or legal requirements for patient or customer confidentiality. The molecular profiling company may bill the individual, insurance provider, medical provider, or government entity for one or more of the following: sample receipt, sample storage, sample preparation, cytological testing, molecular profiling, input and update of sample information into the database, or database access.

[0307] (iii) Business Flow

[0308] FIG. **18***a* is a flow chart illustrating one way in which samples might be processed by the molecular profiling business. Samples of thyroid cells, for example, may be obtained by an endocrinologist perhaps via fine needle aspiration **100**. Samples are subjected to routine cytological staining procedures **125**. Said routine cytological staining provides four different possible preliminary diagnoses non-diagnostic **105**, benign **110**, ambiguous or suspicious **115**, or malignant **120**. The molecular profiling business may then analyze gene expression product levels as described herein **130**. Said analysis of gene expression product levels, molecular profiling, may lead to a definitive diagnosis of malignant **140** or benign **135**. In some cases only a subset of samples are analyzed by molecular profiling such as those that provide ambiguous and non-diagnostic results during routine cytological examination. Alternative embodiments by which samples may be processed by the methods of the present invention are provided in FIGS. **18***b* and **21**.

[0309] In some cases the molecular profiling results confirms the routine cytological test results. In other cases, the molecular profiling results differ. In such cases, samples may be further tested, data may be reexamined, or the molecular profiling results or cytological assay results may be taken as the correct diagnosis. Benign diagnoses may also include diseases or conditions that, while not malignant cancer, may indicate further monitoring or treatment. Similarly, malignant diagnoses may further include diagnosis of the specific type of cancer or a specific metabolic or signaling pathway involved in the disease or condition. Said diagnoses, may

indicate a treatment or therapeutic intervention such as radioactive iodine ablation, surgery, thyroidectomy; or further monitoring.

XI. Kits

[0310] The molecular profiling business may provide a kit for obtaining a suitable sample. Said kit **203** as depicted in FIG. **19** may comprise a container **202**, a means for obtaining a sample **200**, reagents for storing the sample **205**, and instructions for use of said kit. In another embodiment, the kit further comprises reagents and materials for performing the molecular profiling analysis. In some cases, the reagents and materials include a computer program for analyzing the data generated by the molecular profiling methods. In still other cases, the kit contains a means by which the biological sample is stored and transported to a testing facility such as the molecular profiling business or a third party testing center.

[0311] The molecular profiling business may also provide a kit for performing molecular profiling. Said kit may comprise a means for extracting protein or nucleic acids including all necessary buffers and reagents; and, a means for analyzing levels of protein or nucleic acids including controls, and reagents. The kit may further comprise software or a license to obtain and use software for analysis of the data provided using the methods and compositions of the present invention.

EXAMPLES

Example 1

Gene Expression Product Analysis of Thyroid Samples

[0312] 75 thyroid samples were examined for gene expression analysis using the Affymetrix Human Exon 10ST array according to manufacturer's instructions to identify genes that showed significantly differential expression and/or alternative splicing between malignant, benign, and normal samples. Three groups were compared and classified according to pathological surgical diagnosis of the tissue: benign (n=29), malignant (n=37), and normal (n=9). The samples were prepared from surgical thyroid tissue, snap frozen and then the RNA was prepared by standard methods. The names and pathological classification of the 75 samples are depicted in FIG. **1**.

[0313] Microarray analysis was run with XRAY version 2.69 (Biotique Systems Inc.). Input files were normalized with full quantile normalization (Irizarry et al. *Biostatistics* 2003 Apr. 4 (2): 249-64). For each input array and each probe expression value, the array-ith percentile probe value was replaced with the average of all array-ith percentile points. A total of 6,553,590 probes were manipulated in the analysis. Probes with GC count less than 6 and greater than 17 were excluded from the analysis. The expression score for each probe-set was derived via application of median-polish (exon RMA) to the probe scores across all input hybridizations and probe-sets with fewer than 3 probes (that pass all of the tests defined above) were excluded from further analysis. Only 'Core' probe-sets, corresponding to probe-sets matching entries in the high quality databases RefSeq and Ensembl, were analyzed. Non-expressed probes and invariant probes were also removed from analysis for both gene level and probe set level analyses. One-way ANOVA analysis was used to examine gene expression at the probe set level between groups malignant and benign.

[0314] The top 100 differentially expressed genes by gene level analysis (i.e. those genes which showed the greatest differential expression) were obtained from the dataset in which benign malignant and normal thyroid samples were compared. Markers were selected based on statistical significance after Benjamini and Hochberg correction for false discover rate (FDR). An FDR filter value of $p<0.01$ was used, followed by ranking with absolute fold change (>1.9) calculated per maker as the highest differential gene expression value in any group (benign malignant or normal) divided by the lowest differential expression in the remaining two groups. The results of this analysis are shown in FIG. **2**. This table lists three sets of calculated fold changes for any given marker to allow comparison between the groups. The fold changes malignant/benign, malignant/normal, and benign/normal were all calculated by dividing the expression of one group by the expression of another.

[0315] The top 100 alternatively spliced genes were obtained from the dataset in which benign malignant and normal thyroid samples were compared. Markers were selected based on statistical significance after Benjamini and Hochberg correction for false discovery rate (FDR). An FDR filter value of $p<0.01$ was used, and markers were ranked starting with lowest p-value. The threshold for listing a numerical value with the software used was $p<1.0E-301$, any numbers having a smaller p-value were automatically assigned a value of 0.00E+00. The results of this analysis are shown in FIG. **3**. All the markers depicted are highly significant for alternative exon splicing.

[0316] The top 100 differentially expressed genes in the thyroid samples from FIG. **1** by probe-set level analysis were obtained from the dataset in which benign and malignant samples were analyzed. Markers were selected based on significance after Benjamini and Hochberg correction for false discovery rate (FDR). Markers were selected based on significance after Benjamini and Hochberg correction for false discovery rate (FDR). An FDR filter value of $p<0.01$ was used, followed by ranking with absolute fold-change (>2.0) calculated per marker as Malignant expression divided by Benign expression. The results of this analysis are shown in FIG. **4**.

[0317] The top 100 statistically significant diagnostic markers determined by gene level analysis of the thyroid samples shown in FIG. **1** were also compiled. Data from the comparison between benign, malignant, and normal and from comparison between benign and malignant datasets were used. Markers were selected based on significance after Benjamini and Hochberg correction for false discovery rate (FDR). An FDR filter value of $p<0.01$ was used, followed by ranking with absolute fold-change (>1.6) calculated per marker as the highest differential expression value in any group (benign, malignant or normal) divided by the lowest differential expression in the remaining two groups. The fold-changes for Malignant/Benign, Malignant/Normal, and Benign/Normal were all calculated in similar fashion by dividing the expression of one group by the expression of another. The results of this analysis are shown in FIG. **5**.

[0318] The full list of 4918 genes identified as statistically significantly differentially expressed, differentially spliced or both between benign and malignant, benign and normal, or malignant and normal samples at either the probe-set or gene level was also compiled. Markers were selected based

on statistical significance after Benjamini and Hochberg correction for false discovery rate (FDR), and an FDR filter value of $p<0.01$ was used. The results are depicted in FIG. **6**.

Example 2

Gene Expression Product Analysis of Thyroid Tissue Samples

[0319] A total of 205 thyroid tissue samples (FIG. **7**) are examined with an Affymetrix HumanExon10ST array chip to identify genes that differ significantly in RNA expression levels between benign and malignant samples. Samples are classified according to post-surgical thyroid pathology: samples exhibiting follicular adenoma (FA), lymphocytic thyroiditis (LCT), or nodular hyperplasia (NHP) are classified as benign; samples exhibiting Hurthle cell carcinoma (HC), follicular carcinoma (FC), follicular variant of papillary thyroid carcinoma (FVPTC), papillary thyroid carcinoma (PTC), medullary thyroid carcinoma (MTC), or anaplastic carcinoma (ATC) are classified as malignant.

[0320] Affymetrix software is used to extract, normalize, and summarize intensity data from roughly 6.5 million probes. Approximately 280,000 core probe sets are subsequently used in feature selection and classification. The models used are LIMMA for feature selection and random forest and support vector machine (SVM) for classification. Iterative rounds of training, classification, and cross validation are performed using random subsets of data. Top features are identified in two separate analyses (malignant vs. benign and MTC vs. rest) using the classification engine described above.

[0321] Markers are selected based on significance after Benjamini and Hochberg correction for false data discovery rate (FDR). An FDR filter of $p<0.05$ is used.

[0322] A malignant vs. benign comparison of thyroid tissue samples finds 413 markers that are diagnostic for thyroid diseases or conditions. The top 100 markers are listed in FIG. **9**.

[0323] An MTC vs. the rest (i.e. non-MTC) comparison of thyroid tissue samples finds 671 markers that are diagnostic for thyroid diseases or conditions. The top 100 markers are listed in FIG. **10**.

Example 3

Meta-Analysis of Gene Expression Product Data from Thyroid Samples

[0324] Surgical thyroid tissue samples (FIG. **7**) and thyroid samples obtained via fine needle aspiration (FIG. **8**) are identified as benign or malignant by pathological examination and then examined by hybridization to an Affymetrix HumanExon10ST array. A meta-analysis approach is utilized which allows the identification of genes with repeatable features in each classification. Affymetrix software is used to extract, normalize, and summarize intensity data from approximately 6.5 million probes. Roughly 280,000 probe sets are used for feature selection and classification. LIMMA is used for feature selection. Classification is performed with random forest and SVM methods. Markers that repeatedly appear in multiple iterative rounds of training, classification, and cross validation of the surgical and fine needle aspirate samples are identified and ranked. A joint set of core features are created using the top ranked features that appear for both the surgical and fine needle aspirate data. Markers with a non-zero repeatability score are selected as significant. A total of 102 markers are found to be significant and are listed in FIG. **11**.

Example 4

Bayesian Analysis of Gene Expression Product Data from Thyroid Samples

[0325] Two groups of well-characterized samples are compared in order to identify genes that distinguish benign from malignant nodules in the human thyroid. Samples are derived from surgical thyroid tissue (tissue; n=205, FIG. **7**) or from fine needle aspirates (FNA; n=74, FIG. **8**) and are examined by hybridization to the HumanExon10ST microarray. Pathology labels for each distinct thyroid subtype are coded as either benign (B) or malignant (M). A total of 499 markers that show distinct differential expression between benign and malignant samples are identified.

[0326] Affymetrix software is used to extract, normalize, and summarize intensity data from approximately 6.5 million probes. Roughly 280,000 core probe sets are subsequently used in feature selection and classification of ~22,000 genes. The models used are LIMMA (for feature selection) and SVM (for classification) respectively.

[0327] Next, we previously published molecular profile studies are examined in order to derive the type I and type II error rates of assigning a gene into the "benign" or "malignant" category. The error rates are calculated based on the sample size reported in each particular published study with an estimated fold-change value of two. Lastly, these prior probabilities are combined with the output of the Tissue dataset to estimate the posterior probability of differential gene expression, and then combined with the FNA dataset to formulate the final posterior probabilities of differential expression (Smyth 2004). These posterior probabilities are used to rank the genes and those that exceed a posterior probability threshold of 0.9 are selected. A total of 499 markers are identified as significant and the top 100 are listed in FIG. **12**.

Example 5

Subtype Analysis of Gene Expression Product Data from Thyroid Samples

[0328] Well-characterized samples are examined in order to distinguish benign nodules from those with distinct pathology in the human thyroid. 205 hybridizations to the HumanExon10ST microarray are examined. Pathology labels for each distinct thyroid subtype are used to systematically compare one group versus another. A total of 250 mRNA markers that separate thyroid into a wide range of pathology subtypes are identified.

[0329] A total of 205 thyroid tissue samples are examined with the Affymetrix HumanExon10ST array chip to identify genes that differ significantly in mRNA expression between distinct thyroid pathology subtypes (FIG. **7**). Samples classified according to post-surgical thyroid pathology as: follicular adenoma (FA, n=22), lymphocytic thyroiditis (LCT, n=39), nodular hyperplasia (NHP, n=24)), are all collectively classified as benign (n=85). In contrast, samples classified as Hurthle cell carcinoma (HC, n=27), follicular carcinoma (FC, n=19), follicular variant of papillary thyroid carcinoma (FVPTC, n=21), papillary thyroid carcinoma

(PTC, n=26), medullary thyroid carcinoma (MTC, n=22), and anaplastic carcinoma (ATC, n=5) are all collectively classified as malignant (n=120).

[0330] Affymetrix software is used to extract, normalize, and summarize intensity data from roughly 6.5 million probes. Approximately 280,000 core probe sets are subsequently used in feature selection and classification. A given benign subtype (e.g., NHP) set is compared against a pool of all other malignant subtypes (e.g., NHP vs. M) next the benign subset is compared again against each set of malignant subtypes (NHP vs. FC, NHP vs. PTC, etc). The models used in the classification engine are LIMMA (for feature selection), and random forest and SVM are used for classification. Iterative rounds of training, classification, and cross-validation are performed using random subsets of data. A joint core-set of genes that separate distinct thyroid subtypes is created.

[0331] Markers are selected based on the set of genes that optimizes the classifier after pair-wise classification. A total of 251 markers mapping to 250 distinct genes allow the separation of 1-3 distinct thyroid subtypes (FIG. **13**).

Example 6

Differentially Expressed miRNAs Identified Via the Agilent Vs microRNA Array

[0332] Thyroid samples are hybridized to the Agilent Human v2 microRNA (miRNA) array. This array contains probes to 723 human and 76 viral miRNAs, and these are targeted using ~15,000 probesets. A comparison between benign (B) and malignant (M) thyroid samples is performed to identify significant differentially expressed miRNAs. All samples are derived from clinical fine needle aspirates (n=89, FIG. **14**).

[0333] Array intensity data is extracted, normalized, and summarized, followed by modeling using classification engine. Briefly, the models used are LIMMA (for feature selection), and random forest and support vector machine (SVM) are used for classification. Iterative rounds of training, classification, and cross-validation are performed using random subsets of data. Although several miRNAs are differentially expressed in malignant as compared to benign (FIG. **16**), no stand-alone classifiers were identified with this approach.

Example 7

Differentially Expressed miRNAs that are Diagnostic for Thyroid Diseases

[0334] Thyroid nodule samples are hybridized to the Illumina Human v2 miRNA array. This array contains probes to 1146 human miRNAs. A comparison between benign and malignant thyroid samples is performed to identify significant differentially expressed miRNAs. All samples are derived from clinical FNAs (n=24, FIG. **15**).

[0335] Array intensity data is extracted, normalized, and summarized, followed by modeling using a classification engine. Briefly, the models used are LIMMA (for feature selection), and random forest, and support vector machine (SVM) for classification. An additional "hot probes" method is added to the classification engine, which in part incorporates a meta-analysis approach to the algorithm. Iterative rounds of training, classification, and cross-validation are performed using random subsets of data. The "hot probes" method identifies probes that appear in every loop of cross-validation, thereby creating a set of robust, repeatable features. Markers are selected based on the p-value (P) of a comparison between malignant and benign samples. A total of 145 miRNAs are identified whose differential expression is identified as diagnostic for benign or malignant thyroid conditions (FIG. **17**).

Example 8

An Exemplary Device for Molecular Profiling

[0336] The molecular profiling business of the present invention compiles the list of 4918 genes of FIG. **6** that are differentially expressed, differentially spliced or both between benign and malignant, benign and normal, or malignant and normal samples at either the probe-set or the gene level. A subset of the 4918 genes are chosen for use in the diagnosis of biological samples by the molecular profiling business. Compositions of short (i.e. 12-25 nucleotide long) oligonucleotides complimentary to the subset of 4918 genes chose for use by the molecular profiling business are synthesized by standard methods known in the art and immobilized on a solid support such as nitrocellulose, glass, a polymer, or a chip at known positions on the solid support.

Example 9

Molecular Profiling of a Biological Sample

[0337] A biological sample is obtained by fine needle aspiration and stored in two aliquots, one for molecular profiling and one for cytological analysis. The aliquot of biological sample for molecular profiling is added to lysis buffer and triturated which results in lysing of the cells of the biological sample. Lysis buffer is prepared as follows: For 1 ml of cDNA lysis buffer, the following were mixed together on ice: 0.2 ml of Moloney murine leukemia virus (MMLV) reverse transcriptase, 5× (Gibco-BRL), 0.76 ml of H20 (RNAse, DNAse free, Specialty Media), 5 μl of Nonidet P40 (USB), 10 μl of PrimeRNase inhibitor (3'5' Incorporated), 10 μl of RNAguard (Pharmacia), and 20 μl of freshly made, 1/24 dilution of stock primer mix. The stock primer mix, kept aliquoted at −20° C., includes 10 μl each of 100 mM dATP, dCTP, dGTP, dTTP solutions (12.5 mM final)(Boehringer); 10 μl of 50 OD/ml pd(T)19-24 (Pharmacia); and 3 0 μl H20.

[0338] Cell RNA is then primed with an oligo dT primer. Reverse transcription with reverse transcriptase is then performed in limiting conditions of time and reagents to facilitate incomplete extension and to prepare short cDNA of between about 500 bp to about 1000 bp. The cDNA is then tailed at the 5' end with multiple dATP using polyA (dATP) and terminal transferase.

[0339] The cDNA is then amplified with PCR reagents using a 60mer primer having 24(dT) at the 3' end. PCR cycling is performed at 94° C. for 1 minute, then 42° C. for 2 minutes and then 72° C. for 6 minutes with 10 second extension times at each cycle. 10 cycles are performed. Then additional Taq polymerase is added and an additional 25 cycles are performed.

[0340] cDNA is extracted in phenol-chloroform, precipitated with ethanol and then half of the sample is frozen at −80° C. as a stock to avoid thawing and freezing the entire amount of cDNA while analyzing it.

[0341] 5 μg of PCR product is combined with 15.5 μl EF sln (Tris in Qiagen kit PCR purification), 4 μl of lox One-Phor-All buffer from Promega, and 0.5 units of DNase I. The total volume is then held at 37° C. for 14 minutes, then held at 99° C. for 15 minutes and then put on ice for 5 minutes to fragment the PCR product into segments about 50 bp to about 100 bp in length. The fragments are then end-labeled by combining the total volume with 1 μl of Biotin-N6-ddATP ("NEN") and 1.5 μl of TdT (terminal transferase) (15unit/μl). The total volume is then held at 37° C. for 1 hour, then held at 99° C. for 15 minutes and then held on ice for 5 minutes.

[0342] The labeled and fragmented cDNA is hybridized with the probeset of the present invention in 200 microliters of hybridization solution containing 5-10 microgram labeled target in 1×MES buffer (0.1 M MES, 1.0 M NaCl, 0.01% Triton X-100, pH 6.7) and 0.1 mg/ml herring sperm DNA. The arrays used are Affymetrix Human Exon 10ST arrays. The arrays are placed on a rotisserie and rotated at 60 rpm for 16 hours at 45° C. Following hybridization, the arrays are washed with 6×SSPE-T (0.9 M NaCl, 60 mM NaH2P04, 6 mM EDTA, 0.005% Triton X-100, pH 7.6) at 22° C. on a fluidics station (Affymetrix) for 10×2 cycles, and then washed with 0.1 MES at 45° C. for 30 min. The arrays are then stained with a streptavidin-phycoerythrin conjugate (Molecular Probes), followed by 6×SSPE-T wash on the fluidics station for 10×2 cycles again. To enhance the signals, the arrays are further stained with Anti-streptavidin antibody for 30 min followed by a 15 min staining with a streptavidin-phycoerythrin conjugate again. After 6×SSPE-T wash on the fluidics station for 10×2 cycles, the arrays are scanned at a resolution of 3 microns using a modified confocal scanner to determine raw fluorescence intensity values at each position in the array, corresponding to gene expression levels for the sequence at that array position.

[0343] The raw fluorescence intensity values are converted to gene expression product levels, normalized via the RMA method, filtered to remove data that may be considered suspect, and input to a pre-classifier algorithm which corrects the gene expression product levels for the cell-type composition of the biological sample. The corrected gene expression product levels are input to a trained algorithm for classifying the biological sample as benign, malignant, or normal. The trained algorithm provides a record of its output including a diagnosis, and a confidence level.

Example 10

Molecular Profiling of Thyroid Nodule

[0344] An individual notices a lump on his thyroid. The individual consults his family physician. The family physician decides to obtain a sample from the lump and subject it to molecular profiling analysis. Said physician uses a kit from the molecular profiling business to obtain the sample via fine needle aspiration, perform an adequacy test, store the sample in a liquid based cytology solution, and send it to the molecular profiling business. The molecular profiling business divides the sample for cytological analysis of one part and for the remainder of the sample extracts mRNA from the sample, analyzes the quality and suitability of the mRNA sample extracted, and analyses the expression levels and alternative exon usage of a subset of the genes listed in FIG. **5**. In this case, the particular gene expression products profiled is determined by the sample type, by the preliminary diagnosis of the physician, and by the molecular profiling company.

[0345] The molecular profiling business analyses the data and provides a resulting diagnosis to the individual's physician as illustrated in FIG. **20**. The results provide 1) a list of gene expression products profiled, 2) the results of the profiling (e.g. the expression level normalized to an internal standard such as total mRNA or the expression of a well characterized gene product such as tubulin, 3) the gene product expression level expected for normal tissue of matching type, and 4) a diagnosis and recommended treatment for Bob based on the gene product expression levels. The molecular profiling business bills the individual's insurance provider for products and services rendered.

Example 11

Molecular Profiling as an Adjunct to Cytological Examination

[0346] An individual notices a suspicious lump on her thyroid. The individual consults her primary care physician who examines the individual and refers her to an endocrinologist. The endocrinologist obtains a sample via fine needle aspiration, and sends the sample to a cytological testing laboratory. The cytological testing laboratory performs routine cytological testing on a portion of the fine needle aspirate, the results of which are ambiguous (i.e. indeterminate). The cytological testing laboratory suggests to the endocrinologist that the remaining sample may be suitable for molecular profiling, and the endocrinologist agrees.

[0347] The remaining sample is analyzed using the methods and compositions herein. The results of the molecular profiling analysis suggest a high probability of early stage follicular cell carcinoma. The results further suggest that molecular profiling analysis combined with patient data including patient age, and lump or nodule size indicates thyroidectomy followed by radioactive iodine ablation. The endocrinologist reviews the results and prescribes the recommended therapy.

[0348] The cytological testing laboratory bills the endocrinologist for routine cytological tests and for the molecular profiling. The endocrinologist remits payment to the cytological testing laboratory and bills the individual's insurance provider for all products and services rendered. The cytological testing laboratory passes on payment for molecular profiling to the molecular profiling business and withholds a small differential.

Example 12

Molecular Profiling Performed by a Third Party

[0349] An individual complains to her physician about a suspicious lump on her neck. The physician examines the individual, and prescribes a molecular profiling test and a follow up examination pending the results. The individual visits a clinical testing laboratory also known as a CLIA lab. The CLIA lab is licensed to perform molecular profiling of the current invention. The individual provides a sample at the CLIA lab via fine needle aspiration, and the sample is analyzed using the molecular profiling methods and compositions herein. The results of the molecular profiling are electronically communicated to the individual's physician,

and the individual is contacted to schedule a follow up examination. The physician presents the results of the molecular profiling to the individual and prescribes a therapy.

Example 13

Overlapping Genes Using Different Analysis Methods

[0350] The results described in Example 2 were obtained by examining surgical thyroid nodule tissue samples and comparing gene expression in malignant versus benign ("malignant vs. benign" data set). This analysis identified 412 genes that are differentially expressed (FDR $p<0.05$). In a previous study described in Example 1, using i) a different cohort of samples and ii) a different analysis method, we describe 4918 genes that can distinguish between malignant and benign thyroid nodules ("4918"). The "malignant vs. benign" tissue discovery dataset shares 231/412 genes with the "4918" discovery dataset, while 181/412 genes have been newly discovered.

[0351] A similar comparison between medullary thyroid cancer (MTC) and the "Rest" of the thyroid subtypes using the tissue cohort pointed to 668 significant genes that are differentially expressed between these two groups (FIG. **10**). When cross-checked against our previous "4918" gene list, we note that 305/668 genes had been previously described, while 363/668 genes have been newly discovered.

[0352] We next combined the surgical tissue dataset with a fine needle aspirate (FNA) dataset and once again compared malignant versus benign using i) a "hot probes" and ii) a "Bayes" approach. Each analysis identified 102 and 498 significant genes, respectively (Tables 11 and 12).

[0353] Up until this point a total of 1343 significant genes were identified. However, a subsequent subset analysis aimed at identifying those genes that separate distinct pathology subtypes from one another was also performed. This analysis used the surgical tissue cohort and resulted in 250 significant genes (FIG. **13**).

[0354] In sum, the five comparisons described here give rise to 1437 significant genes. Of these, 636/1437 genes are described for the first time as distinguishing malignant versus benign thyroid pathology. As of today, 568/636 have not yet been described in published scientific literature or patent applications as diagnostic markers of thyroid cancer.

Example 14

Clinical Thyroid FNA

[0355] Methods

[0356] Prospective clinical thyroid FNA samples were examined with the Affymetrix Human Exon 1.0ST microarray in order to identify genes that differ significantly in mRNA expression between benign and malignant samples.

[0357] Affymetrix software was used to extract, normalize, and summarize intensity data from roughly 6.5 million probes. Approximately 280,000 core probe sets were subsequently used in feature selection and classification. The models used were LIMMA (for feature selection), random forest and SVM were used for classification (Smyth 2004; Diaz-Uriarte and Alvarez de Andres 2006). Iterative rounds of training, classification, and cross-validation were performed using random subsets of data. Top features were identified in three separate analyses using the classification engine described above.

[0358] While the annotation and mapping of genes to transcript cluster indentifiers (TCID) is constantly evolving, the nucleotide sequences in the probesets that make up a TCID do not change. Furthermore, a number of significant TCIDs do not map any known genes, yet these are equally important biomarkers in the classification of thyroid malignancy. Results are described using both the TCID and the genes currently mapped to each (Affymetrix annotation file: HuEx-1_0-st-v2.na29.hg18.transcript.csv).

[0359] Results

[0360] The study of differential gene expression in prospectively collected, clinical thyroid FNA required a number of statistical sub-analyses. These sub-analyses alone resulted in the discovery of genes that are valuable in the classification of thyroid nodules of unknown pathology. However, the joining of the datasets has resulted in the novel characterization of thyroid gene panels, which can correctly classify thyroid FNA with improved accuracy over current cytopathology, and molecular profiling methods.

TABLE 3

Top Benign vs. Malignant Analysis.

TCID	Gene Symbol (Affy v.na29)	FDR LIMMA p-value	Fold Change
2884845	GABRB2	2.85E−35	3.22
2400177	CAMK2N1	8.23E−30	2.50
3638204	MFGE8	2.16E−29	1.75
3638204	QTRT1	2.16E−29	1.75
2708855	C11orf72	4.11E−27	2.27
2708855	LIPH	4.11E−27	2.27
3415744	IGFBP6	5.44E−27	1.81
3136178	PLAG1	1.64E−26	1.76
2657808	CLDN16	3.63E−26	3.01
3451375	PRICKLE1	3.63E−26	1.78
2442008	RXRG	7.62E−26	2.17
3329343	MDK	3.60E−24	1.34
3666366	CDH3	3.60E−24	1.25
3757108	KRT19	1.06E−23	1.44
3040518	MACC1	1.14E−23	1.73
3988596	ZCCHC12	2.14E−23	2.22
3416895	METTL7B	2.90E−23	1.33
2721959	ROS1	6.26E−23	3.05
2721959	SLC34A2	6.26E−23	3.05
3125116	DLC1	9.12E−23	0.82
2828441	PDLIM4	9.51E−23	0.81
2783596	PDE5A	1.60E−22	1.93
3645555	TNFRSF12A	1.71E−22	1.25
3973891	CXorf27	1.75E−22	1.38
3973891	SYTL5	1.75E−22	1.38
2827645	SLC27A6	2.02E−22	2.28
3020343	MET	2.02E−22	2.25
3452478	AMIGO2	2.03E−22	1.17
2451931	GOLT1A	2.15E−22	0.84
3679959	EMP2	3.81E−22	1.51
3417249	ERBB3	1.11E−21	1.05
3087167	TUSC3	1.16E−21	1.90
2924492	HEY2	1.38E−21	1.38
2685304	PROS1	1.48E−21	2.15
3335894	CST6	1.50E−21	2.50
3393720	MPZL2	1.52E−21	1.86
3907234	SDC4	1.60E−21	1.64
4012178	CITED1	4.03E−21	2.42
2994981	PRR15	5.89E−21	0.94
2973232	C6orf174	6.09E−21	1.07
2973232	KIAA0408	6.09E−21	1.07
2809245	ITGA2	6.13E−21	1.84
3067478	NRCAM	9.01E−21	1.70

TABLE 3-continued

Top Benign vs. Malignant Analysis.

TCID	Gene Symbol (Affy v.na29)	FDR LIMMA p-value	Fold Change
3420316	HMGA2	1.13E−20	0.94
4018327	TRPC5	1.14E−20	1.78
3416921	RDH5	1.24E−20	0.55
2333318	PTPRF	1.42E−20	0.78
3336486	C11orf80	1.71E−20	0.58
3336486	RCE1	1.71E−20	0.58
3044072	NOD1	3.06E−20	1.01
3417809	NAB2	3.40E−20	0.57
2710599	CLDN1	4.47E−20	2.53
3343452	FZD4	4.93E−20	1.49
3343452	PRSS23	4.93E−20	1.49
2720584	SLIT2	6.84E−20	1.45
3389976	SLC35F2	1.16E−19	0.94
3587495	SCG5	1.45E−19	1.60
3744463	MYH10	1.58E−19	1.40
3987607	CCDC121	1.87E−19	1.56
3987607	ZCCHC16	1.87E−19	1.56
3984945	ARMCX3	3.69E−19	1.11
2558612	TGFA	9.18E−19	0.89
3522398	AIDA	1.02E−18	1.33
3522398	DOCK9	1.02E−18	1.33
2781736	CFI	1.04E−18	1.91
3338192	CCND1	1.09E−18	1.25
3338192	FLJ42258	1.09E−18	1.25
2414958	TACSTD2	1.12E−18	0.91
2991860	ITGB8	1.51E−18	1.30
2805078	CDH6	1.64E−18	1.58
3976341	TIMP1	1.98E−18	1.68
2562435	EDNRB	1.98E−18	1.61
2562435	SFTPB	1.98E−18	1.61
3726154	ITGA3	2.04E−18	1.17
2381249	C1orf115	4.38E−18	0.92
2356818	BCL9	6.05E−18	0.63
3451814	MAFG	7.13E−18	1.92
3451814	NELL2	7.13E−18	1.92
3445908	EPS8	7.19E−18	1.60
2451870	ETNK2	8.68E−18	1.00
3201345	LOC554202	1.08E−17	1.05
3581221	AHNAK2	1.14E−17	1.28
2966193	C6orf168	1.23E−17	0.85
2876608	CXCL14	1.85E−17	1.76
3129065	CLU	1.85E−17	1.37
3222170	TNC	1.94E−17	1.24
2438458	CRABP2	2.16E−17	1.24
2600689	EPHA4	2.17E−17	1.51
3763390	TMEM100	2.61E−17	1.34
2902958	C4A	3.56E−17	1.36
2902958	C4B	3.56E−17	1.36
2952834	KCNK5	6.07E−17	0.51
2452478	LEMD1	9.66E−17	1.27
3751002	RAB34	1.14E−16	0.83
3489138	CYSLTR2	1.72E−16	1.61
2417362	DIRAS3	1.72E−16	1.15
2370123	XPR1	1.81E−16	0.89
2680046	ADAMTS9	1.83E−16	1.40
3494629	SCEL	2.04E−16	1.61
3040967	RAPGEF5	2.04E−16	0.92
3554452	KIAA0284	2.33E−16	0.59
4020655	ODZ1	2.44E−16	1.97
2400518	ECE1	3.31E−16	0.98
2598261	FN1	3.58E−16	2.41
3187686	GSN	4.03E−16	0.78
2742224	SPRY1	3.51E−15	1.18
3628832	DAPK2	4.59E−15	1.17
3408831	SSPN	4.69E−15	0.99
3925639	NRIP1	5.01E−15	1.02
3683377	GPRC5B	5.39E−15	1.10
2397025	DHRS3	5.83E−15	1.14
2816298	IQGAP2	6.56E−15	−1.04
3848039	C3	7.85E−15	1.62
3367673	MPPED2	7.93E−15	−1.71
2822215	PAM	8.70E−15	1.08

TABLE 3-continued

Top Benign vs. Malignant Analysis.

TCID	Gene Symbol (Affy v.na29)	FDR LIMMA p-value	Fold Change
2567167	LONRF2	1.12E−14	1.40
2522094	SPATS2L	2.21E−14	0.96
3898355	FLRT3	2.70E−14	1.96
3717870	TMEM98	2.72E−14	1.51
3212008	FRMD3	3.50E−14	1.43
2597867	IKZF2	3.58E−14	0.91
3007960	CLDN4	6.44E−14	1.27
2468811	ASAP2	7.11E−14	0.89
3046197	ELMO1	8.04E−14	−1.10
3132616	ZMAT4	8.04E−14	−1.29
3181600	GALNT12	8.25E−14	0.74
3095313	C8orf4	8.38E−14	1.28
2525533	LOC648149	8.38E−14	1.01
2525533	MAP2	8.38E−14	1.01
3464860	DUSP6	9.39E−14	1.10
3464860	LOC100131490	9.39E−14	1.10
2751936	GALNT7	1.52E−13	0.93
2578790	LRP1B	1.65E−13	−1.33
2700365	TM4SF1	2.19E−13	1.60
2598828	IGFBP5	2.87E−13	1.67
3126191	PSD3	3.12E−13	1.34
3979101	FAAH2	3.88E−13	0.68
3577612	SERPINA1	3.99E−13	1.12
3577612	SERPINA2	3.99E−13	1.12
3622934	MYEF2	4.25E−13	0.92
3622934	SLC24A5	4.25E−13	0.92
2738664	SGMS2	4.47E−13	1.13
3692999	MT1G	4.65E−13	−2.43
2902844	C2	7.40E−13	1.36
2902844	CFB	7.40E−13	1.36
3662201	MT1F	8.84E−13	−1.87
3662201	MT1H	8.84E−13	−1.87
3662201	MT1P2	8.84E−13	−1.87
2617188	ITGA9	1.07E−12	1.05
3401704	CCND2	1.09E−12	0.86
2562529	ST3GAL5	1.34E−12	0.88
2371139	LAMC2	1.53E−12	0.99
2626802	PTPRG	1.83E−12	1.06
2834282	STK32A	2.53E−12	1.23
2526806	FN1	3.12E−12	1.84
3111561	MAPK6	3.66E−12	−2.04
3111561	PKHD1L1	3.66E−12	−2.04
3238962	KIAA1217	7.24E−12	1.21
3238962	PRINS	7.24E−12	1.21
3110608	TM7SF4	7.72E−12	1.92
2466554	TPO	1.14E−11	−1.78
3126368	PSD3	2.30E−11	1.39
3558418	STXBP6	3.35E−11	0.94
2980449	IPCEF1	3.42E−11	−1.05
3907190	SLPI	4.25E−11	1.61
2955932	GPR110	5.17E−11	1.29
2976360	PERP	7.31E−11	1.31
2686023	DCBLD2	8.03E−11	0.98
2915828	NT5E	9.40E−11	1.19
3219621	CTNNAL1	1.17E−10	1.01
3971451	PHEX	1.39E−10	1.53
3417583	RBMS2	1.39E−10	1.09
2424102	CNN3	1.58E−10	1.07
3369931	RAG2	2.12E−10	−1.41
2730746	SLC4A4	2.24E−10	−1.21
3010503	CD36	2.91E−10	−1.42
3446137	LMO3	3.09E−10	1.44
3933536	TFF3	3.09E−10	−1.10
4021777	IGSF1	3.11E−10	1.55
3467949	SLC5A8	4.08E−10	−1.34
3288518	C10orf72	4.26E−10	1.18
2336891	DIO1	4.31E−10	−1.73
2498274	C2orf40	4.39E−10	1.71
2740067	ANK2	5.52E−10	−0.90
2924330	TPD52L1	6.04E−10	1.09
2427469	SLC16A4	6.71E−10	1.37
2727587	KIT	1.23E−09	−1.24

TABLE 3-continued

Top Benign vs. Malignant Analysis.

TCID	Gene Symbol (Affy v.na29)	FDR LIMMA p-value	Fold Change
3464417	MGAT4C	1.45E−09	1.26
2331558	BMP8A	3.61E−09	−1.55
2711205	ATP13A4	6.51E−09	1.15
3142381	FABP4	7.25E−09	−1.59
3743551	CLDN7	8.01E−09	1.13
3662150	MT1M	8.06E−09	−1.47
3662150	MT1P3	8.06E−09	−1.47

TABLE 3-continued

Top Benign vs. Malignant Analysis.

TCID	Gene Symbol (Affy v.na29)	FDR LIMMA p-value	Fold Change
3166644	TMEM215	9.05E−09	1.51
3087659	SLC7A2	1.32E−08	1.28
3321055	TEAD1	1.37E−07	1.10
3059667	SEMA3D	1.43E−07	−1.83

[0361] This analysis resulted in 175 unique TCIDs, currently mapping to 198 genes.

TABLE 4

Top Subtype Analysis

TCID	Gene Symbol (Affy vna29)	Subtype 1	Subtype 2	Subtype 3	Subtype 4
3153400	3153400	NHP_PTC			
3749600	3749600	NHP_PTC			
3726691	ABCC3		FA_FVPTC		
3368940	ABTB2	NHP_PTC			
3279058	ACBD7	NHP_PTC			
2796553	ACSL1	NHP_PTC			
3299504	ACTA2	NHP_PTC			
3927480	ADAMTS5	NHP_PTC			
2680046	ADAMTS9	NHP_PTC	FA_FVPTC	NHP_FVPTC	LCT_REST
3252170	ADK	NHP_PTC			
3039791	AGR2	NHP_PTC			
3581221	AHNAK2	NHP_PTC			
2991233	AHR	NHP_PTC			
3522398	AIDA	NHP_PTC		NHP_FVPTC	
3226138	AK1	NHP_PTC			
3233049	AKR1C3			NHP_FVPTC	
4009849	ALAS2	NHP_PTC			
3611625	ALDH1A3	NHP_PTC			
3169331	ALDH1B1		FA_FVPTC		
3571727	ALDH6A1		FA_FVPTC		
3452478	AMIGO2	NHP_PTC			
4018454	AMOT	NHP_PTC			
2740067	ANK2	NHP_PTC		NHP_FVPTC	
3323748	ANO5		FA_FVPTC	NHP_FVPTC	
3174816	ANXA1	NHP_PTC			
2732844	ANXA3	NHP_PTC			
2881747	ANXA6			NHP_FVPTC	
3046062	AOAH	NHP_PTC			
2455418	AP3S1	NHP_PTC			
4002809	APOO		FA_FVPTC	NHP_FVPTC	
3595594	AQP9	NHP_PTC			
2734421	ARHGAP24	NHP_PTC			
2632453	ARL13B	NHP_PTC			
2931391	ARL4A	NHP_PTC			
3984945	ARMCX3	NHP_PTC			
4015838	ARMCX6	NHP_PTC			
3321150	ARNTL	NHP_PTC			
3768474	ARSG			NHP_FVPTC	
2468811	ASAP2	NHP_PTC			
2526759	ATIC	NHP_PTC			
2711225	ATP13A4	NHP_PTC			
2711205	ATP13A4	NHP_PTC			
3105749	ATP6V0D2			NHP_FVPTC	
3824596	B3GNT3	NHP_PTC			
2356818	BCL9	NHP_PTC			
2608725	BHLHE40	NHP_PTC			
3448088	BHLHE41	NHP_PTC			
3772187	BIRC5				LCT_REST
2331558	BMP8A	NHP_PTC		NHP_FVPTC	
3926080	BTG3	NHP_PTC			
3288518	C10orf72		FA_FVPTC	NHP_FVPTC	
2708855	C11orf72	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3327166	C11orf74		FA_FVPTC	NHP_FVPTC	
3336486	C11orf80	NHP_PTC			
3473331	C12orf49	NHP_PTC			

TABLE 4-continued

Top Subtype Analysis					
TCID	Gene Symbol (Affy vna29)	Subtype 1	Subtype 2	Subtype 3	Subtype 4
3571727	C14orf45		FA_FVPTC		
3649714	C16orf45	NHP_PTC			
3832280	C19orf33	NHP_PTC			
2381249	C1orf115	NHP_PTC			
2453065	C1orf116	NHP_PTC			
2902844	C2	NHP_PTC			
3963676	C22orf9			NHP_FVPTC	
2498274	C2orf40	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3848039	C3	NHP_PTC			
2902958	C4A	NHP_PTC	FA_FVPTC	NHP_FVPTC	
2902958	C4B	NHP_PTC	FA_FVPTC	NHP_FVPTC	
2766492	C4orf34	NHP_PTC			
2730303	C4orf7				LCT_REST
2855578	C5orf28		FA_FVPTC		
2966193	C6orf168	NHP_PTC			
2973232	C6orf174	NHP_PTC	FA_FVPTC		
3060450	C7orf62	NHP_PTC			
3095313	C8orf4	NHP_PTC			
3086809	C8orf79		FA_FVPTC		
3867264	CA11	NHP_PTC			
3392332	CADM1	NHP_PTC			
2400177	CAMK2N1	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3420713	CAND1	NHP_PTC			
3020302	CAV1	NHP_PTC			
3020273	CAV2	NHP_PTC			
3987607	CCDC121	NHP_PTC	FA_FVPTC	NHP_FVPTC	
2582701	CCDC148	NHP_PTC			
2688813	CCDC80	NHP_PTC			
3718204	CCL13	NHP_PTC			
3204285	CCL19				LCT_REST
3338192	CCND1	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3380065	CCND1			NHP_FVPTC	
3401704	CCND2	NHP_PTC		NHP_FVPTC	
3316344	CD151	NHP_PTC			
2860178	CD180				LCT_REST
2636125	CD200	NHP_PTC			
3010503	CD36	NHP_PTC		NHP_FVPTC	
3834502	CD79A				LCT_REST
2671728	CDCP1	NHP_PTC			
3694657	CDH11	NHP_PTC			
3666366	CDH3	NHP_PTC	FA_FVPTC		
2805078	CDH6	NHP_PTC			
3417146	CDK2	NHP_PTC			
2773719	CDKL2	NHP_PTC			
2871896	CDO1	NHP_PTC			
4024373	CDR1	NHP_PTC			
2902844	CFB	NHP_PTC			
2373336	CFH	NHP_PTC			
2373336	CFHR1	NHP_PTC			
2781736	CFI	NHP_PTC			
3920003	CHAF1B	NHP_PTC			
3442054	CHD4	NHP_PTC			
4012178	CITED1	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3178583	CKS2	NHP_PTC			
3862108	CLC	NHP_PTC			
2710599	CLDN1	NHP_PTC		NHP_FVPTC	
3497195	CLDN10	NHP_PTC			
2657808	CLDN16	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3007960	CLDN4	NHP_PTC		NHP_FVPTC	
3743551	CLDN7	NHP_PTC			
3443183	CLEC4E	NHP_PTC			
3129065	CLU	NHP_PTC	FA_FVPTC		
2424102	CNN3	NHP_PTC			
3762198	COL1A1	NHP_PTC			
3761054	COPZ2		FA_FVPTC	NHP_FVPTC	
3106559	CP	NHP_PTC			
3105904	CPNE3		FA_FVPTC		
2377283	CR2				LCT_REST
3603295	CRABP1	NHP_PTC			
2438458	CRABP2	NHP_PTC	FA_FVPTC		
2406783	CSF3R	NHP_PTC			
3126504	CSGALNACT1		FA_FVPTC		

TABLE 4-continued

Top Subtype Analysis

TCID	Gene Symbol (Affy vna29)	Subtype 1	Subtype 2	Subtype 3	Subtype 4
3335894	CST6	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3219621	CTNNAL1	NHP_PTC			
2618940	CTNNB1	NHP_PTC			
3634811	CTSH	NHP_PTC			
3338552	CTTN	NHP_PTC			
2773434	CXCL1	NHP_PTC			
2732508	CXCL13				LCT_REST
2876608	CXCL14	NHP_PTC			
3863640	CXCL17	NHP_PTC			
2773434	CXCL2	NHP_PTC			
2773434	CXCL3	NHP_PTC			
4024420	CXorf18	NHP_PTC			
3973891	CXorf27	NHP_PTC			
3910429	CYP24A1			NHP_FVPTC	
2528093	CYP27A1			NHP_FVPTC	
3489138	CYSLTR2	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3628832	DAPK2	NHP_PTC	FA_FVPTC	NHP_FVPTC	
2686023	DCBLD2	NHP_PTC			
3683845	DCUN1D3	NHP_PTC			
2420832	DDAH1	NHP_PTC			
3329649	DDB2	NHP_PTC			
3754736	DDX52	NHP_PTC			
3487095	DGKH	NHP_PTC			
3074912	DGKI	NHP_PTC			
3558118	DHRS1	NHP_PTC			
2397025	DHRS3	NHP_PTC			
2336891	DIO1	NHP_PTC	FA_FVPTC	NHP_FVPTC	
2417362	DIRAS3	NHP_PTC		NHP_FVPTC	
3125116	DLC1	NHP_PTC	FA_FVPTC		
3522398	DOCK9	NHP_PTC		NHP_FVPTC	
3913483	DPH3B		FA_FVPTC		
2584018	DPP4	NHP_PTC			
2880292	DPYSL3	NHP_PTC			
3783529	DSG2	NHP_PTC			
2893794	DSP	NHP_PTC			
2958325	DST	NHP_PTC			
3622176	DUOX1			NHP_FVPTC	
3622176	DUOX2			NHP_FVPTC	
3622239	DUOXA1			NHP_FVPTC	
3622239	DUOXA2			NHP_FVPTC	
3129731	DUSP4	NHP_PTC			
3263743	DUSP5	NHP_PTC			
3464860	DUSP6	NHP_PTC			
3497195	DZIP1	NHP_PTC			
2400518	ECE1	NHP_PTC	FA_FVPTC	NHP_FVPTC	
2562435	EDNRB	NHP_PTC			
3002640	EGFR	NHP_PTC			
2484970	EHBP1	NHP_PTC			
3837431	EHD2	NHP_PTC			
3326461	EHF	NHP_PTC			
3544387	EIF2B2		FA_FVPTC		
3427098	ELK3	NHP_PTC			
3046197	ELMO1	NHP_PTC			
3679959	EMP2	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3852832	EMR3	NHP_PTC			
2458338	ENAH	NHP_PTC			
3345427	ENDOD1	NHP_PTC			
2327677	EPB41	NHP_PTC			
2600689	EPHA4	NHP_PTC			
2346625	EPHX4	NHP_PTC			
3772187	EPR1				LCT_REST
3445908	EPS8	NHP_PTC			
3720402	ERBB2		FA_FVPTC		
3417249	ERBB3	NHP_PTC			
3683845	ERI2	NHP_PTC			
2462329	ERO1LB		FA_FVPTC		
3445768	ERP27	NHP_PTC			
2451870	ETNK2	NHP_PTC			
3039177	ETV1	NHP_PTC			
2709132	ETV5	NHP_PTC			
2863363	F2RL2	NHP_PTC			
3979101	FAAH2	NHP_PTC			

TABLE 4-continued

		Top Subtype Analysis			
TCID	Gene Symbol (Affy vna29)	Subtype 1	Subtype 2	Subtype 3	Subtype 4
3142381	FABP4	NHP_PTC		NHP_FVPTC	
3331926	FAM111A	NHP_PTC			
3331903	FAM111B	NHP_PTC			
3104323	FAM164A	NHP_PTC			
2560625	FAM176A	NHP_PTC			
3768535	FAM20A	NHP_PTC			
3143330	FAM82B		FA_FVPTC		
3152558	FAM84B	NHP_PTC			
2396750	FBXO2	NHP_PTC			
3473480	FBXO21	NHP_PTC			
3229338	FCN1	NHP_PTC			
3229338	FCN2	NHP_PTC			
2742109	FGF2	NHP_PTC			
3413950	FGFR1OP2	NHP_PTC			
3324447	FIBIN		FA_FVPTC		
2738244	FLJ20184	NHP_PTC			
3346147	FLJ32810	NHP_PTC			
3338192	FLJ42258	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3380065	FLJ42258			NHP_FVPTC	
3898355	FLRT3	NHP_PTC			
2526806	FN1	NHP_PTC			
2598261	FN1	NHP_PTC	FA_FVPTC		
3869237	FPR1	NHP_PTC			
3839910	FPR2	NHP_PTC			
3212008	FRMD3	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3393479	FXYD6			NHP_FVPTC	
3343452	FZD4	NHP_PTC			
3110272	FZD6	NHP_PTC			
2523045	FZD7	NHP_PTC			
3217242	GABBR2	NHP_PTC			
2884845	GABRB2	NHP_PTC	FA_FVPTC	NHP_FVPTC	
2341083	GADD45A	NHP_PTC			
2401581	GALE	NHP_PTC			
3181600	GALNT12	NHP_PTC			
2585129	GALNT3	NHP_PTC			
2751936	GALNT7	NHP_PTC			
2684187	GBE1			NHP_FVPTC	
2421843	GBP1	NHP_PTC			
2421843	GBP3	NHP_PTC			
3044129	GGCT	NHP_PTC			
4015763	GLA			NHP_FVPTC	
3593931	GLDN	NHP_PTC			
2417272	GNG12	NHP_PTC			
2451931	GOLT1A	NHP_PTC			
2955932	GPR110	NHP_PTC			
2955999	GPR110	NHP_PTC			
2819779	GPR98	NHP_PTC		NHP_FVPTC	
3683377	GPRC5B	NHP_PTC			
2827057	GRAMD3	NHP_PTC			
3187686	GSN	NHP_PTC			
2787958	GYPB	NHP_PTC			
2504328	GYPC	NHP_PTC			
2787958	GYPE	NHP_PTC			
2809793	GZMK				LCT_REST
3217077	HEMGN	NHP_PTC			
2924492	HEY2	NHP_PTC	FA_FVPTC	NHP_FVPTC	
2946194	HIST1H1A	NHP_PTC			
2946215	HIST1H3B				LCT_REST
2947081	HIST1H4L				LCT_REST
2950125	HLA-DQB2	NHP_PTC			
3420316	HMGA2	NHP_PTC			
3830065	HPN	NHP_PTC			
2658275	HRASLS		FA_FVPTC		
3508330	HSPH1	NHP_PTC			
3820443	ICAM1	NHP_PTC			
2401493	ID3		FA_FVPTC		
2708922	IGF2BP2		FA_FVPTC		
2598828	IGFBP5	NHP_PTC			
3415744	IGFBP6	NHP_PTC	FA_FVPTC	NHP_FVPTC	
4021777	IGSF1	NHP_PTC	FA_FVPTC		
2597867	IKZF2		FA_FVPTC	NHP_FVPTC	
3755862	IKZF3		FA_FVPTC		

TABLE 4-continued

Top Subtype Analysis					
TCID	Gene Symbol (Affy vna29)	Subtype 1	Subtype 2	Subtype 3	Subtype 4
2497082	IL1RL1	NHP_PTC			
3275729	IL2RA			NHP_FVPTC	
2731332	IL8			NHP_FVPTC	
2599303	IL8RA	NHP_PTC			
2599303	IL8RB	NHP_PTC			
2527580	IL8RB	NHP_PTC			
2599303	IL8RBP	NHP_PTC			
2527580	IL8RBP	NHP_PTC			
2673873	IMPDH2	NHP_PTC			
3267382	INPP5F	NHP_PTC			
2980449	IPCEF1	NHP_PTC			
2816298	IQGAP2	NHP_PTC			
2809245	ITGA2	NHP_PTC			
3726154	ITGA3	NHP_PTC			
2617188	ITGA9	NHP_PTC	FA_FVPTC		
3852832	ITGB1	NHP_PTC			
2583465	ITGB6	NHP_PTC			
2991860	ITGB8	NHP_PTC			
4013549	ITM2A				LCT_REST
2608469	ITPR1	NHP_PTC			
3556990	JUB	NHP_PTC			
3998766	KAL1	NHP_PTC			
2628260	KBTBD8				LCT_REST
2952834	KCNK5	NHP_PTC			
3154002	KCNQ3	NHP_PTC			
3383130	KCTD14	NHP_PTC			
2827525	KDELC1	NHP_PTC			
3945314	KDELR3	NHP_PTC			
2959039	KHDRBS2	NHP_PTC			
3554452	KIAA0284	NHP_PTC		NHP_FVPTC	
2973232	KIAA0408	NHP_PTC	FA_FVPTC		
3238962	KIAA1217	NHP_PTC		NHP_FVPTC	
3529951	KIAA1305		FA_FVPTC		
2727587	KIT	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3978943	KLF8	NHP_PTC			
2708066	KLHL6				LCT_REST
3868828	KLK10	NHP_PTC			
3868783	KLK7	NHP_PTC			
3415576	KRT18	NHP_PTC			
3757108	KRT19	NHP_PTC	FA_FVPTC		
2453793	LAMB3	NHP_PTC			
2371065	LAMC1	NHP_PTC			
2371139	LAMC2	NHP_PTC			
2962026	LCA5	NHP_PTC			
3653619	LCMT1	NHP_PTC			
3190190	LCN2	NHP_PTC			
4024420	LDOC1	NHP_PTC			
2452478	LEMD1	NHP_PTC			
2854092	LIFR		FA_FVPTC		
3841545	LILRA1	NHP_PTC			
3841545	LILRB1	NHP_PTC			
3454331	LIMA1	NHP_PTC			
3202528	LINGO2	NHP_PTC			
2708855	LIPH	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3446137	LMO3	NHP_PTC	FA_FVPTC	NHP_FVPTC	
2345286	LMO4	NHP_PTC			
3028011	LOC100124692	NHP_PTC			
3442054	LOC100127974	NHP_PTC			
3765689	LOC100129112	NHP_PTC			
3759587	LOC100129115	NHP_PTC			
2601414	LOC100129171	NHP_PTC			
2577482	LOC100129961	NHP_PTC			
2504328	LOC100130248	NHP_PTC			
3110272	LOC100131102	NHP_PTC			
3464860	LOC100131490	NHP_PTC			
2364677	LOC100131938	NHP_PTC			
3922793	LOC100132338	NHP_PTC			
3392332	LOC100132764	NHP_PTC			
3487095	LOC283508	NHP_PTC			
3724698	LOC440434	NHP_PTC			
3201345	LOC554202	NHP_PTC			
2455418	LOC643454	NHP_PTC			

TABLE 4-continued

Top Subtype Analysis					
TCID	Gene Symbol (Affy vna29)	Subtype 1	Subtype 2	Subtype 3	Subtype 4
2525533	LOC648149	NHP_PTC			
4015838	LOC653354	NHP_PTC			
3724698	LOC653498	NHP_PTC			
2936857	LOC730031	NHP_PTC			
2567167	LONRF2	NHP_PTC			LCT_REST
2872848	LOX	NHP_PTC			
3220384	LPAR1			NHP_FVPTC	
3442137	LPAR5	NHP_PTC			
3088486	LPL	NHP_PTC			
2578790	LRP1B	NHP_PTC		NHP_FVPTC	
3106559	LRRC69	NHP_PTC			
2608309	LRRN1	NHP_PTC			
3465248	LUM	NHP_PTC			
3683845	LYRM1	NHP_PTC			
3040518	MACC1	NHP_PTC	FA_FVPTC		
3451814	MAFG	NHP_PTC	FA_FVPTC		
3994710	MAMLD1	NHP_PTC			
2525533	MAP2	NHP_PTC			
3111561	MAPK6	NHP_PTC		NHP_FVPTC	
3108526	MATN2		FA_FVPTC		
2539607	MBOAT2	NHP_PTC			
3097152	MCM4	NHP_PTC			
3063685	MCM7	NHP_PTC			
3329343	MDK	NHP_PTC	FA_FVPTC		
2962820	ME1			NHP_FVPTC	
3765689	MED13	NHP_PTC			
3020343	MET	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3416895	METTL7B	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3808096	MEX3C	NHP_PTC			
3638204	MFGE8	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3028011	MGAM	NHP_PTC			
2890859	MGAT1			NHP_FVPTC	
3464417	MGAT4C	NHP_PTC			
2658275	MGC2889		FA_FVPTC		
3406589	MGST1	NHP_PTC			
3707759	MIS12		FA_FVPTC		
2936857	MLLT4	NHP_PTC			
3143660	MMP16	NHP_PTC			
3143643	MMP16	NHP_PTC			
2362333	MNDA	NHP_PTC			
4017212	MORC4	NHP_PTC			
3367673	MPPED2	NHP_PTC			
3393720	MPZL2	NHP_PTC	FA_FVPTC	NHP_FVPTC	
2955025	MRPL14	NHP_PTC			
3662201	MT1F	NHP_PTC	FA_FVPTC		
3692999	MT1G	NHP_PTC		NHP_FVPTC	
3662201	MT1H	NHP_PTC	FA_FVPTC		
3662150	MT1M	NHP_PTC			
3662201	MT1P2	NHP_PTC	FA_FVPTC		
3662150	MT1P3	NHP_PTC			
2931391	MTHFD1L	NHP_PTC			
2437118	MUC1	NHP_PTC			
3366903	MUC15	NHP_PTC			
3655723	MVP	NHP_PTC			
3997825	MXRA5	NHP_PTC			
3622934	MYEF2	NHP_PTC			
3744463	MYH10	NHP_PTC			
2520429	MYO1B	NHP_PTC			
3752709	MYO1D	NHP_PTC			
3624607	MYO5A			NHP_FVPTC	
2914070	MYO6	NHP_PTC			
3417809	NAB2	NHP_PTC			
3695268	NAE1	NHP_PTC			
3074912	NAG20	NHP_PTC			
3323052	NAV2		FA_FVPTC	NHP_FVPTC	
3349293	NCAM1		FA_FVPTC		
2590736	NCKAP1	NHP_PTC			
3495076	NDFIP2	NHP_PTC			
3789947	NEDD4L	NHP_PTC			
3451814	NELL2	NHP_PTC	FA_FVPTC		
2343231	NEXN	NHP_PTC			
3456666	NFE2	NHP_PTC			

TABLE 4-continued

Top Subtype Analysis					
TCID	Gene Symbol (Affy vna29)	Subtype 1	Subtype 2	Subtype 3	Subtype 4
3199207	NFIB	NHP_PTC			
2325410	NIPAL3	NHP_PTC			
3182957	NIPSNAP3A		FA_FVPTC		
3182957	NIPSNAP3B		FA_FVPTC		
3044072	NOD1	NHP_PTC	FA_FVPTC		
3571904	NPC2	NHP_PTC			
3724698	NPEPPS	NHP_PTC			
2370926	NPL			NHP_FVPTC	
2792127	NPY1R	NHP_PTC			
3067478	NRCAM	NHP_PTC		NHP_FVPTC	
3925639	NRIP1	NHP_PTC			
2524301	NRP2	NHP_PTC			
2915828	NT5E	NHP_PTC			
3143330	NTAN1		FA_FVPTC		
3322251	NUCB2		FA_FVPTC	NHP_FVPTC	
2742109	NUDT6	NHP_PTC			
3654699	NUPR1		FA_FVPTC		
2768654	OCIAD2	NHP_PTC			
2375338	OCR1	NHP_PTC			
4020655	ODZ1	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3380065	ORAOV1			NHP_FVPTC	
3801621	OSBPL1A			NHP_FVPTC	
3555461	OSGEP	NHP_PTC			
2807359	OSMR	NHP_PTC			
2701071	P2RY13	NHP_PTC			
2875193	P4HA2	NHP_PTC			
2822215	PAM	NHP_PTC			
3256590	PAPSS2			NHP_FVPTC	
3505781	PARP4	NHP_PTC			
3320865	PARVA	NHP_PTC			
2364677	PBX1	NHP_PTC			
3134922	PCMTD1		FA_FVPTC		
2783596	PDE5A	NHP_PTC		NHP_FVPTC	
3922793	PDE9A	NHP_PTC			
3087703	PDGFRL	NHP_PTC			
3301218	PDLIM1	NHP_PTC			
2828441	PDLIM4	NHP_PTC			
3411810	PDZRN4	NHP_PTC			
3013255	PEG10	NHP_PTC			
2976360	PERP	NHP_PTC			
3971451	PHEX	NHP_PTC			
3975893	PHF16	NHP_PTC			
2635906	PHLDB2	NHP_PTC			
3127385	PHYHIP	NHP_PTC			
3811086	PIGN		FA_FVPTC		
3111561	PKHD1L1	NHP_PTC		NHP_FVPTC	
2511820	PKP4	NHP_PTC			
3376529	PLA2G16	NHP_PTC			
2955827	PLA2G7			NHP_FVPTC	
2583374	PLA2R1	NHP_PTC			
3136178	PLAG1	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3252036	PLAU	NHP_PTC			
3759587	PLCD3	NHP_PTC			
2521574	PLCL1			NHP_FVPTC	
3867458	PLEKHA4	NHP_PTC			
3407096	PLEKHA5	NHP_PTC			
2858023	PLK2	NHP_PTC			
3987996	PLS3	NHP_PTC			
3911217	PMEPA1	NHP_PTC			
3061997	PON2	NHP_PTC			
2763550	PPARGC1A	NHP_PTC			
2773358	PPBP	NHP_PTC			
3678462	PPL	NHP_PTC			
2931090	PPP1R14C	NHP_PTC			
3384270	PRCP			NHP_FVPTC	
3451375	PRICKLE1	NHP_PTC			
3238962	PRINS	NHP_PTC		NHP_FVPTC	
2682271	PROK2	NHP_PTC			
2685304	PROS1	NHP_PTC			
2994981	PRR15	NHP_PTC			
3973692	PRRG1	NHP_PTC			
3343452	PRSS23	NHP_PTC			

TABLE 4-continued

		Top Subtype Analysis			
TCID	Gene Symbol (Affy vna29)	Subtype 1	Subtype 2	Subtype 3	Subtype 4
3175971	PSAT1		FA_FVPTC		
3126368	PSD3	NHP_PTC			
3126191	PSD3	NHP_PTC			
2455418	PTPN14	NHP_PTC			
2333318	PTPRF	NHP_PTC			
2626802	PTPRG	NHP_PTC			
2973376	PTPRK	NHP_PTC			
3757917	PTRF	NHP_PTC			
3134922	PXDNL		FA_FVPTC		
3638204	QTRT1	NHP_PTC	FA_FVPTC	NHP_FVPTC	
2361257	RAB25	NHP_PTC			
3625271	RAB27A	NHP_PTC			
2929699	RAB32			NHP_FVPTC	
3751002	RAB34	NHP_PTC			
3183757	RAD23B	NHP_PTC			
3369931	RAG2	NHP_PTC	FA_FVPTC		
4001223	RAI2	NHP_PTC			
3040967	RAPGEF5	NHP_PTC			
3456081	RARG	NHP_PTC			
2819044	RASA1	NHP_PTC			
3944210	RASD2	NHP_PTC			
4000944	RBBP7	NHP_PTC			
3781429	RBBP8	NHP_PTC			
3417583	RBMS2	NHP_PTC			
3336486	RCE1	NHP_PTC			
3416921	RDH5	NHP_PTC			
2779335	RG9MTD2		FA_FVPTC		
2372812	RGS13				LCT_REST
2372719	RGS18	NHP_PTC			
2372858	RGS2	NHP_PTC			
2384401	RHOU	NHP_PTC			
2580802	RND3	NHP_PTC			
2721959	ROS1	NHP_PTC	FA_FVPTC	NHP_FVPTC	
2709606	RPL39L	NHP_PTC			
3804143	RPRD1A	NHP_PTC			
3867965	RRAS	NHP_PTC			
2469252	RRM2				LCT_REST
2442008	RXRG	NHP_PTC	FA_FVPTC	NHP_FVPTC	
2435981	S100A12	NHP_PTC			
4045665	S100A14	NHP_PTC			
4045643	S100A16	NHP_PTC			
2435989	S100A8	NHP_PTC			
2359664	S100A9	NHP_PTC			
3691326	SALL1	NHP_PTC		NHP_FVPTC	
3564027	SAV1	NHP_PTC			
2750594	SC4MOL	NHP_PTC			
3091475	SCARA3	NHP_PTC			
3442054	SCARNA11	NHP_PTC			
3494629	SCEL	NHP_PTC			
3587495	SCG5	NHP_PTC		NHP_FVPTC	
3441885	SCNN1A	NHP_PTC			
3043895	SCRN1	NHP_PTC			
3907234	SDC4	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3779756	SEH1L	NHP_PTC			
2443450	SELL	NHP_PTC			
3058759	SEMA3C			NHP_FVPTC	
3059667	SEMA3D	NHP_PTC			
2732273	SEPT11	NHP_PTC			
2328273	SERINC2	NHP_PTC			
3577612	SERPINA1	NHP_PTC	FA_FVPTC		
3577612	SERPINA2	NHP_PTC	FA_FVPTC		
2601414	SERPINE2	NHP_PTC			
3331355	SERPING1	NHP_PTC			
2326774	SFN	NHP_PTC			
2562435	SFTPB	NHP_PTC			
2768981	SGCB	NHP_PTC			
3061805	SGCE	NHP_PTC			
2648535	SGEF	NHP_PTC			
2738664	SGMS2	NHP_PTC			
3088213	SH2D4A	NHP_PTC			
3304970	SH3PXD2A	NHP_PTC			
3894727	SIRPA	NHP_PTC			

TABLE 4-continued

		Top Subtype Analysis			
TCID	Gene Symbol (Affy vna29)	Subtype 1	Subtype 2	Subtype 3	Subtype 4
3894727	SIRPB1	NHP_PTC			
3154263	SLA	NHP_PTC			
2827525	SLC12A2	NHP_PTC			
2427469	SLC16A4	NHP_PTC			
3768412	SLC16A6			NHP_FVPTC	
2960955	SLC17A5	NHP_PTC			
3622934	SLC24A5	NHP_PTC			
3018605	SLC26A4	NHP_PTC			
3106559	SLC26A7	NHP_PTC			
3593575	SLC27A2	NHP_PTC			
2827645	SLC27A6	NHP_PTC			
2721959	SLC34A2	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3216276	SLC35D2		FA_FVPTC		
3389976	SLC35F2	NHP_PTC			
3804195	SLC39A6	NHP_PTC			
2730746	SLC4A4	NHP_PTC			
3467949	SLC5A8	NHP_PTC			
2786322	SLC7A11		FA_FVPTC	NHP_FVPTC	
3087659	SLC7A2	NHP_PTC			
2720584	SLIT2	NHP_PTC			
3907190	SLPI	NHP_PTC			
3509842	SMAD9		FA_FVPTC		
2937144	SMOC2	NHP_PTC			
3766960	SMURF2	NHP_PTC			
2777714	SNCA	NHP_PTC			
3597857	SNX1	NHP_PTC			
3597914	SNX22	NHP_PTC			
2348437	SNX7	NHP_PTC			
2369557	SOAT1			NHP_FVPTC	
2797202	SORBS2	NHP_PTC			
3413950	SPATS2	NHP_PTC			
2522094	SPATS2L	NHP_PTC			
2585933	SPC25				LCT_REST
3590164	SPINT1	NHP_PTC			
2556752	SPRED2	NHP_PTC			
2742224	SPRY1	NHP_PTC	FA_FVPTC		
3519309	SPRY2	NHP_PTC			
3677969	SRL	NHP_PTC			
3408831	SSPN	NHP_PTC			
2562529	ST3GAL5	NHP_PTC			
3011861	STEAP2		FA_FVPTC		
2834282	STK32A	NHP_PTC		NHP_FVPTC	
3558418	STXBP6			NHP_FVPTC	
3102372	SULF1	NHP_PTC			
2979871	SYNE1	NHP_PTC			
2378256	SYT14	NHP_PTC			
3973891	SYTL5	NHP_PTC			
2414958	TACSTD2	NHP_PTC			
3898126	TASP1		FA_FVPTC		
3724698	TBC1D3F	NHP_PTC			
3264621	TCF7L2		FA_FVPTC		
3913483	TCFL5		FA_FVPTC		
2435218	TDRKH	NHP_PTC			
3320944	TEAD1	NHP_PTC			
3321055	TEAD1	NHP_PTC			
2573570	TFCP2L1	NHP_PTC			
3933536	TFF3	NHP_PTC			
2591421	TFPI			NHP_FVPTC	
2558612	TGFA	NHP_PTC			
2380590	TGFB2	NHP_PTC			
3181728	TGFBR1	NHP_PTC			
3976341	TIMP1	NHP_PTC	FA_FVPTC		
2649113	TIPARP	NHP_PTC			
3615579	TJP1	NHP_PTC			
3173880	TJP2	NHP_PTC			
3751042	TLCD1	NHP_PTC			
3969115	TLR8	NHP_PTC			
2700365	TM4SF1	NHP_PTC			
2647315	TM4SF4	NHP_PTC			
3110608	TM7SF4	NHP_PTC			
3763390	TMEM100	NHP_PTC			
3412345	TMEM117	NHP_PTC			

TABLE 4-continued

Top Subtype Analysis

TCID	Gene Symbol (Affy vna29)	Subtype 1	Subtype 2	Subtype 3	Subtype 4
3346147	TMEM133	NHP_PTC			
2577482	TMEM163	NHP_PTC			
2815220	TMEM171		FA_FVPTC	NHP_FVPTC	
3166644	TMEM215	NHP_PTC		NHP_FVPTC	
3571904	TMEM90A	NHP_PTC			
3717870	TMEM98	NHP_PTC			
3351200	TMPRSS4	NHP_PTC			
3222170	TNC	NHP_PTC			
3150455	TNFRSF11B		FA_FVPTC		
3645555	TNFRSF12A	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3648391	TNFRSF17				LCT_REST
3222128	TNFSF15	NHP_PTC			
3907111	TOMM34	NHP_PTC			
3136888	TOX				LCT_REST
2924330	TPD52L1	NHP_PTC			
2466554	TPO	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3818515	TRIP10	NHP_PTC			
4018327	TRPC5	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3512294	TSC22D1	NHP_PTC			
2991150	TSPAN13	NHP_PTC			
4015397	TSPAN6	NHP_PTC			
3891342	TUBB1	NHP_PTC			
3779579	TUBB6	NHP_PTC			
3401217	TULP3	NHP_PTC			
3087167	TUSC3	NHP_PTC			
3809324	TXNL1		FA_FVPTC		
3429460	TXNRD1			NHP_FVPTC	
3775842	TYMS	NHP_PTC			
2448971	UCHL5			NHP_FVPTC	
2974592	VNN1			NHP_FVPTC	
2974635	VNN2	NHP_PTC			
2974610	VNN3	NHP_PTC			
3203855	WDR40A	NHP_PTC			
2489228	WDR54	NHP_PTC			
3625052	WDR72		FA_FVPTC		
3768474	WIPI1			NHP_FVPTC	
2677356	WNT5A	NHP_PTC			
4015548	XKRX	NHP_PTC			
2370123	XPR1	NHP_PTC			
3832280	YIF1B	NHP_PTC			
2413484	YIPF1		FA_FVPTC		
4024373	YTHDC2	NHP_PTC			
3989089	ZBTB33	NHP_PTC			
3988596	ZCCHC12	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3987607	ZCCHC16	NHP_PTC	FA_FVPTC	NHP_FVPTC	
3569754	ZFP36L1	NHP_PTC			
2706791	ZMAT3	NHP_PTC			
3132616	ZMAT4	NHP_PTC	FA_FVPTC	NHP_FVPTC	
2331903	ZNF643	NHP_PTC			
3011675	ZNF804B	NHP_PTC			

[0362] This analysis resulted in 599 unique TCIDs, currently mapping to 681 genes.

TABLE 5

Trident Analysis

TCID	Gene Symbol (Affy v.na29)	Repeatable	Bayes	Tissue	DE	P value
3393720	MPZL2	TRUE	TRUE	TRUE	1.49	1.87E-32
2400177	CAMK2N1	TRUE	TRUE	FALSE	1.67	2.27E-29
3067478	NRCAM	TRUE	TRUE	FALSE	1.42	2.53E-29
3445908	EPS8	TRUE	TRUE	TRUE	1.44	6.34E-29
3020343	MET	TRUE	TRUE	FALSE	1.49	1.47E-27
4012178	CITED1	TRUE	TRUE	FALSE	1.50	2.37E-27
2710599	CLDN1	TRUE	TRUE	FALSE	1.41	9.07E-27
3338192	CCND1	TRUE	TRUE	TRUE	1.36	2.63E-26

TABLE 5-continued

Trident Analysis

TCID	Gene Symbol (Affy v.na29)	Repeatable	Bayes	Tissue	DE	P value
3338192	FLJ42258	TRUE	TRUE	TRUE	1.36	2.63E−26
3126191	PSD3	TRUE	TRUE	TRUE	1.32	3.49E−25
2884845	GABRB2	TRUE	TRUE	FALSE	1.73	4.07E−25
3087167	TUSC3	TRUE	TRUE	FALSE	1.49	6.22E−25
3907234	SDC4	TRUE	TRUE	FALSE	1.46	2.08E−24
2721959	ROS1	TRUE	TRUE	FALSE	1.48	2.82E−24
2721959	SLC34A2	TRUE	TRUE	FALSE	1.48	2.82E−24
3679959	EMP2	FALSE	TRUE	FALSE	1.50	2.83E−24
2708855	C11orf72	TRUE	TRUE	TRUE	1.59	1.31E−23
2708855	LIPH	TRUE	TRUE	TRUE	1.59	1.31E−23
3416895	METTL7B	TRUE	TRUE	FALSE	1.49	2.12E−23
3136178	PLAG1	FALSE	TRUE	TRUE	1.41	2.37E−23
2442008	RXRG	TRUE	TRUE	FALSE	1.60	3.50E−23
2657808	CLDN16	TRUE	TRUE	TRUE	1.51	2.63E−22
3984945	ARMCX3	TRUE	TRUE	FALSE	1.45	3.13E−22
2567167	LONRF2	TRUE	TRUE	TRUE	1.38	3.67E−22
2685304	PROS1	TRUE	TRUE	FALSE	1.46	3.81E−22
3744463	MYH10	TRUE	TRUE	FALSE	1.46	6.20E−22
3415744	IGFBP6	TRUE	TRUE	FALSE	1.56	9.91E−22
2834282	STK32A	TRUE	TRUE	TRUE	1.27	1.03E−21
3554452	KIAA0284	TRUE	TRUE	FALSE	1.32	1.38E−21
3040518	MACC1	TRUE	TRUE	FALSE	1.47	1.42E−21
3587495	SCG5	TRUE	TRUE	FALSE	1.34	1.74E−21
2686023	DCBLD2	TRUE	TRUE	FALSE	1.18	1.83E−21
3335894	CST6	FALSE	TRUE	FALSE	1.43	2.29E−21
2783596	PDE5A	TRUE	TRUE	TRUE	1.55	2.63E−21
3522398	AIDA	TRUE	TRUE	FALSE	1.38	2.99E−21
3522398	DOCK9	TRUE	TRUE	FALSE	1.38	2.99E−21
3638204	MFGE8	TRUE	TRUE	FALSE	1.51	5.35E−21
3638204	QTRT1	TRUE	TRUE	FALSE	1.51	5.35E−21
3323052	NAV2	TRUE	TRUE	FALSE	1.30	7.00E−21
2924492	HEY2	TRUE	TRUE	FALSE	1.48	2.01E−20
3726154	ITGA3	TRUE	TRUE	FALSE	1.35	2.16E−20
2924330	TPD52L1	TRUE	TRUE	FALSE	1.17	2.21E−20
3988596	ZCCHC12	TRUE	TRUE	FALSE	1.52	2.85E−20
3683377	GPRC5B	TRUE	TRUE	FALSE	1.28	4.84E−20
3417249	ERBB3	FALSE	TRUE	FALSE	1.51	6.63E−20
2511820	PKP4	TRUE	TRUE	TRUE	1.22	7.51E−20
4020655	ODZ1	TRUE	TRUE	FALSE	1.34	8.32E−20
3628832	DAPK2	FALSE	TRUE	FALSE	1.34	1.20E−19
3007960	CLDN4	TRUE	TRUE	FALSE	1.20	1.42E−19
2598261	FN1	TRUE	TRUE	FALSE	1.31	3.25E−19
2936857	LOC730031	TRUE	TRUE	TRUE	1.12	5.16E−19
2936857	MLLT4	TRUE	TRUE	TRUE	1.12	5.16E−19
3666366	CDH3	TRUE	TRUE	TRUE	1.48	6.10E−19
3757108	KRT19	TRUE	TRUE	FALSE	1.41	6.20E−19
3451375	PRICKLE1	FALSE	TRUE	TRUE	1.42	8.79E−19
3338552	CTTN	TRUE	TRUE	TRUE	1.10	9.53E−19
2680046	ADAMTS9	TRUE	TRUE	FALSE	1.40	1.06E−18
3867458	PLEKHA4	TRUE	TRUE	FALSE	1.35	1.50E−18
3494629	SCEL	TRUE	TRUE	FALSE	1.39	1.57E−18
3978943	KLF8	TRUE	TRUE	FALSE	1.35	3.66E−18
2397025	DHRS3	TRUE	TRUE	FALSE	1.22	3.89E−18
3420316	HMGA2	TRUE	TRUE	TRUE	1.48	4.63E−18
3126368	PSD3	TRUE	TRUE	FALSE	1.19	5.77E−18
2809245	ITGA2	TRUE	TRUE	FALSE	1.45	6.16E−18
2526806	FN1	TRUE	TRUE	TRUE	1.19	7.55E−18
2827645	SLC27A6	FALSE	TRUE	FALSE	1.49	8.33E−18
3217361	ANKS6	TRUE	TRUE	FALSE	1.19	8.37E−18
3743551	CLDN7	TRUE	TRUE	FALSE	1.07	1.80E−17
3571904	NPC2	FALSE	TRUE	FALSE	0.99	2.53E−17
3571904	TMEM90A	FALSE	TRUE	FALSE	0.99	2.53E−17
2558612	TGFA	TRUE	TRUE	FALSE	1.35	2.71E−17
3987607	CCDC121	TRUE	TRUE	FALSE	1.46	3.28E−17
3987607	ZCCHC16	TRUE	TRUE	FALSE	1.46	3.28E−17
3088213	SH2D4A	TRUE	TRUE	FALSE	1.18	5.07E−17
3751002	RAB34	TRUE	TRUE	FALSE	1.19	5.77E−17
3973891	CXorf27	TRUE	TRUE	FALSE	1.52	6.03E−17
3973891	SYTL5	TRUE	TRUE	FALSE	1.52	6.03E−17
3044072	NOD1	TRUE	TRUE	TRUE	1.45	6.85E−17
2370123	XPR1	TRUE	TRUE	FALSE	1.26	7.13E−17
3174816	ANXA1	FALSE	TRUE	TRUE	1.08	7.85E−17

TABLE 5-continued

Trident Analysis

TCID	Gene Symbol (Affy v.na29)	Repeatable	Bayes	Tissue	DE	P value
2966193	C6orf168	TRUE	TRUE	FALSE	1.37	1.01E−16
2525533	LOC648149	TRUE	TRUE	FALSE	1.24	1.02E−16
2525533	MAP2	TRUE	TRUE	FALSE	1.24	1.02E−16
3154002	KCNQ3	TRUE	TRUE	FALSE	1.41	1.09E−16
3590164	SPINT1	TRUE	TRUE	FALSE	1.17	1.35E−16
3329343	MDK	TRUE	TRUE	TRUE	1.28	1.58E−16
2875193	P4HA2	TRUE	TRUE	FALSE	1.10	1.80E−16
3726691	ABCC3	TRUE	TRUE	FALSE	1.17	1.86E−16
2451870	ETNK2	TRUE	TRUE	TRUE	1.33	1.91E−16
4018327	TRPC5	TRUE	TRUE	TRUE	1.48	2.43E−16
3046197	ELMO1	TRUE	TRUE	TRUE	−1.26	2.80E−16
2460817	SIPA1L2	TRUE	TRUE	TRUE	1.17	3.16E−16
3976341	TIMP1	TRUE	TRUE	TRUE	1.15	3.39E−16
2973232	C6orf174	TRUE	TRUE	FALSE	1.42	3.78E−16
2973232	KIAA0408	TRUE	TRUE	FALSE	1.42	3.78E−16
3417809	NAB2	TRUE	TRUE	FALSE	1.25	5.50E−16
2751936	GALNT7	TRUE	TRUE	FALSE	1.17	5.95E−16
2648535	SGEF	TRUE	FALSE	FALSE	1.16	1.33E−15
3759587	LOC100129115	TRUE	TRUE	FALSE	1.34	1.47E−15
3759587	PLCD3	TRUE	TRUE	FALSE	1.34	1.47E−15
3994710	MAMLD1	FALSE	TRUE	FALSE	1.37	1.80E−15
3581221	AHNAK2	TRUE	TRUE	FALSE	1.31	2.29E−15
3259253	C10orf131	FALSE	TRUE	TRUE	1.01	4.17E−15
3259253	ENTPD1	FALSE	TRUE	TRUE	1.01	4.17E−15
2562435	EDNRB	FALSE	TRUE	FALSE	1.37	5.28E−15
2562435	SFTPB	FALSE	TRUE	FALSE	1.37	5.28E−15
3489138	CYSLTR2	TRUE	TRUE	TRUE	1.30	5.69E−15
3002640	EGFR	TRUE	TRUE	TRUE	1.11	8.20E−15
2578790	LRP1B	FALSE	TRUE	FALSE	−0.95	1.06E−14
3768535	FAM20A	FALSE	TRUE	FALSE	1.25	1.11E−14
3044129	GGCT	TRUE	TRUE	FALSE	1.11	1.12E−14
2980449	IPCEF1	TRUE	TRUE	TRUE	−1.14	1.29E−14
4018454	AMOT	TRUE	TRUE	FALSE	1.34	1.47E−14
3763390	TMEM100	TRUE	TRUE	TRUE	1.40	2.44E−14
2740067	ANK2	FALSE	TRUE	TRUE	−0.89	2.57E−14
3622934	MYEF2	TRUE	TRUE	TRUE	1.03	4.13E−14
3622934	SLC24A5	TRUE	TRUE	TRUE	1.03	4.13E−14
2414958	TACSTD2	FALSE	TRUE	FALSE	1.29	5.50E−14
3321150	ARNTL	TRUE	TRUE	TRUE	1.18	7.68E−14
3464860	DUSP6	TRUE	TRUE	FALSE	1.10	1.17E−13
3464860	LOC100131490	TRUE	TRUE	FALSE	1.10	1.17E−13
3217242	GABBR2	TRUE	TRUE	TRUE	1.21	1.22E−13
3110608	TM7SF4	TRUE	TRUE	TRUE	1.23	2.16E−13
3110395	RIMS2	TRUE	TRUE	FALSE	1.13	2.54E−13
3649714	C16orf45	TRUE	TRUE	FALSE	1.10	7.74E−13
3867264	CA11	TRUE	TRUE	FALSE	1.05	8.23E−13
3832280	C19orf33	TRUE	TRUE	FALSE	1.20	8.77E−13
3832280	YIF1B	TRUE	TRUE	FALSE	1.20	8.77E−13
2452440	KLHDC8A	TRUE	TRUE	FALSE	1.08	1.39E−12
2608469	ITPR1	TRUE	TRUE	TRUE	−1.10	1.71E−12
3577612	SERPINA1	FALSE	TRUE	FALSE	0.96	2.24E−12
3577612	SERPINA2	FALSE	TRUE	FALSE	0.96	2.24E−12
4015548	XKRX	TRUE	TRUE	FALSE	1.12	2.68E−12
3451814	MAFG	FALSE	TRUE	TRUE	1.04	2.91E−12
3451814	NELL2	FALSE	TRUE	TRUE	1.04	2.91E−12
2734421	ARHGAP24	FALSE	TRUE	FALSE	−1.05	3.17E−12
2816298	IQGAP2	TRUE	TRUE	FALSE	−1.10	5.75E−12
2524301	NRP2	FALSE	TRUE	FALSE	0.93	7.41E−12
3132616	ZMAT4	FALSE	TRUE	TRUE	−0.89	1.03E−11
3365136	SERGEF	FALSE	TRUE	TRUE	0.98	1.04E−11
3367673	MPPED2	FALSE	TRUE	FALSE	−0.95	1.18E−11
2608309	LRRN1	FALSE	FALSE	TRUE	0.84	1.66E−11
2820925	RHOBTB3	FALSE	TRUE	TRUE	0.85	2.73E−11
3369931	RAG2	FALSE	TRUE	TRUE	−0.75	3.90E−11
2708922	IGF2BP2	FALSE	TRUE	TRUE	0.90	5.15E−11
3868783	KLK7	TRUE	TRUE	TRUE	1.19	7.94E−11
3006572	AUTS2	TRUE	TRUE	FALSE	1.06	1.02E−10
3411810	PDZRN4	TRUE	TRUE	FALSE	1.20	1.21E−10
2876897	SPOCK1	TRUE	FALSE	FALSE	1.05	1.39E−10
3166644	TMEM215	FALSE	FALSE	TRUE	0.98	1.49E−10
3933536	TFF3	FALSE	TRUE	FALSE	−0.80	2.50E−10
3159330	DOCK8	FALSE	TRUE	TRUE	−0.90	2.53E−10

TABLE 5-continued

Trident Analysis

TCID	Gene Symbol (Affy v.na29)	Repeatable	Bayes	Tissue	DE	P value
3279058	ACBD7	FALSE	TRUE	TRUE	1.03	2.83E−10
3593931	GLDN	TRUE	TRUE	FALSE	1.13	3.46E−10
3404030	KLRG1	FALSE	TRUE	TRUE	−0.88	5.39E−10
2373842	PTPRC	FALSE	FALSE	TRUE	−0.90	9.75E−10
3010503	CD36	FALSE	TRUE	TRUE	−0.81	3.46E−09
2583374	PLA2R1	FALSE	TRUE	TRUE	−0.72	6.14E−09
3856646	ZNF208	FALSE	FALSE	TRUE	0.77	6.91E−09
3692999	MT1G	FALSE	TRUE	TRUE	−0.82	1.01E−08
2587790	GPR155	FALSE	TRUE	FALSE	−0.86	1.12E−08
2362351	PYHIN1	FALSE	FALSE	TRUE	−0.76	1.46E−08
2727587	KIT	FALSE	TRUE	FALSE	−0.75	1.50E−08
2427619	KCNA3	FALSE	FALSE	TRUE	−0.78	1.50E−08
3142381	FABP4	FALSE	TRUE	FALSE	−0.72	1.82E−08
2584018	DPP4	FALSE	TRUE	TRUE	0.78	2.22E−08
2387126	RYR2	FALSE	TRUE	TRUE	−0.64	2.26E−08
2823880	CAMK4	FALSE	FALSE	TRUE	−0.72	2.67E−08
3410384	C12orf35	FALSE	FALSE	TRUE	−0.78	2.74E−08
2466554	TPO	FALSE	TRUE	FALSE	−0.77	5.30E−08
2806468	IL7R	FALSE	FALSE	TRUE	−0.78	1.04E−07
2730746	SLC4A4	FALSE	TRUE	TRUE	−0.73	1.12E−07
3467949	SLC5A8	FALSE	FALSE	TRUE	−0.74	1.23E−07
2518272	CERKL	FALSE	FALSE	TRUE	−0.74	1.58E−07
2518272	ITGA4	FALSE	FALSE	TRUE	−0.74	1.58E−07
3450861	ABCD2	FALSE	FALSE	TRUE	−0.66	1.63E−07
3389450	CARD16	FALSE	FALSE	TRUE	−0.78	1.66E−07
3389450	CASP1	FALSE	FALSE	TRUE	−0.78	1.66E−07
2657831	IL1RAP	FALSE	TRUE	FALSE	0.78	1.85E−07
3059667	SEMA3D	FALSE	TRUE	TRUE	−0.71	2.04E−07
4013460	CYSLTR1	FALSE	FALSE	TRUE	−0.71	2.12E−07
3126504	CSGALNACT1	FALSE	TRUE	TRUE	−0.65	2.29E−07
3811339	BCL2	FALSE	TRUE	TRUE	−0.76	2.29E−07
2724671	RHOH	FALSE	FALSE	TRUE	−0.69	2.37E−07
3160895	JAK2	FALSE	FALSE	TRUE	−0.74	2.48E−07
2486811	PLEK	FALSE	FALSE	TRUE	−0.75	2.66E−07
3443804	KLRB1	FALSE	FALSE	TRUE	−0.73	2.84E−07
3576704	TC2N	FALSE	TRUE	TRUE	−0.74	3.29E−07
3742627	C17orf87	FALSE	FALSE	TRUE	−0.70	4.80E−07
3347658	ATM	FALSE	FALSE	TRUE	−0.65	4.89E−07
3347658	NPAT	FALSE	FALSE	TRUE	−0.65	4.89E−07
2815220	TMEM171	FALSE	FALSE	TRUE	−0.60	5.00E−07
3960174	LGALS2	FALSE	FALSE	TRUE	−0.70	5.58E−07
2462329	ERO1LB	FALSE	TRUE	TRUE	−0.67	6.74E−07
2608725	BHLHE40	FALSE	TRUE	TRUE	0.72	8.08E−07
3389353	CARD17	FALSE	FALSE	TRUE	−0.72	1.09E−06
3389353	CASP1	FALSE	FALSE	TRUE	−0.72	1.09E−06
3062082	PDK4	FALSE	FALSE	TRUE	0.67	1.22E−06
2593159	STK17B	FALSE	FALSE	TRUE	−0.65	1.88E−06
2353669	CD2	FALSE	FALSE	TRUE	−0.67	2.06E−06
2428796	PTPN22	FALSE	FALSE	TRUE	−0.66	2.70E−06
2422035	GBP5	FALSE	FALSE	TRUE	−0.69	3.37E−06
2766289	TMEM156	FALSE	FALSE	TRUE	−0.57	4.55E−06
3060450	C7orf62	FALSE	FALSE	TRUE	−0.61	5.81E−06
2439554	AIM2	FALSE	FALSE	TRUE	−0.60	6.78E−06
3443891	CLEC2B	FALSE	FALSE	TRUE	−0.58	3.51E−05
2766192	TLR10	FALSE	FALSE	TRUE	−0.51	3.87E−05
3536706	LGALS3	FALSE	TRUE	FALSE	0.52	4.67E−05
3009838	CCDC146	FALSE	FALSE	TRUE	−0.56	7.30E−05
3009838	POLR2J4	FALSE	FALSE	TRUE	−0.56	7.30E−05
2412312	TTC39A	FALSE	FALSE	TRUE	0.51	7.45E−05
2548699	CYP1B1	FALSE	TRUE	FALSE	0.49	3.52E−04
3443868	CD69	FALSE	FALSE	TRUE	−0.47	4.85E−04
3461981	TSPAN8	FALSE	FALSE	TRUE	−0.44	7.33E−04
3648391	TNFRSF17	FALSE	FALSE	TRUE	−0.44	7.66E−04
3018605	SLC26A4	FALSE	TRUE	TRUE	−0.46	9.81E−04
3107828	PLEKHF2	FALSE	FALSE	TRUE	−0.42	1.19E−03
2372812	RGS13	FALSE	FALSE	TRUE	−0.38	1.66E−03
3197955	GLDC	FALSE	FALSE	TRUE	−0.37	5.51E−03
2796995	SORBS2	FALSE	FALSE	TRUE	−0.32	1.01E−02
3135567	LYPLA1	FALSE	FALSE	TRUE	−0.32	1.78E−02
2732508	CXCL13	FALSE	FALSE	TRUE	−0.30	1.94E−02
3200982	MLLT3	FALSE	FALSE	TRUE	−0.30	2.03E−02
2735027	SPP1	FALSE	FALSE	TRUE	0.25	6.47E−02

TABLE 5-continued

Trident Analysis

TCID	Gene Symbol (Affy v.na29)	Repeatable	Bayes	Tissue	DE	P value
2554018	EFEMP1	FALSE	FALSE	TRUE	−0.20	1.55E−01
2945882	CMAH	FALSE	FALSE	TRUE	−0.21	1.65E−01
2767378	ATP8A1	FALSE	FALSE	TRUE	0.20	1.79E−01
4016193	TMSB15A	FALSE	FALSE	TRUE	−0.16	2.27E−01
4016193	TMSB15B	FALSE	FALSE	TRUE	−0.16	2.27E−01
3019158	LRRN3	FALSE	FALSE	TRUE	0.16	2.57E−01
2700244	CP	FALSE	FALSE	TRUE	0.12	4.37E−01
2700244	HPS3	FALSE	FALSE	TRUE	0.12	4.37E−01
2855285	CCDC152	FALSE	FALSE	TRUE	−0.10	4.49E−01
2855285	SEPP1	FALSE	FALSE	TRUE	−0.10	4.49E−01
2773947	CXCL9	FALSE	FALSE	TRUE	−0.10	4.56E−01
3108226	PGCP	FALSE	TRUE	TRUE	0.04	7.65E−01
2773972	CXCL11	FALSE	FALSE	TRUE	0.02	8.93E−01

[0363] This benign vs. malignant analysis resulted in 210 unique TCIDs, currently mapping to 237 genes. These genes represent the union of three statistically significant sub-analyses (Repeatable, Bayes, and Tissue) using a single dataset.

[0364] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

What is claimed is:

1. A method of detecting a thyroid condition in a subject comprising:

(a) obtaining a sample of thyroid from said subject;

(b) assaying expression levels of three or more gene expression products in a sample of thyroid tissue obtained from said subject, which gene expression products correspond to at least three genes or corresponding Transcript Cluster ID Nos selected from AKT1, PIK3CA, PTEN, NTRK3 and ALK;

(c) using a computer to classify said sample of thyroid tissue as benign or normal by applying an algorithm to said expression levels from (a), wherein said classifying is based on an expression level in said sample of thyroid tissue of said at least three genes or corresponding Transcript Cluster ID Nos selected from AKT1, PIK3CA, PTEN, NTRK3 and ALK;

(d) generating an electronic report upon classifying said sample of thyroid tissue, which electronic report is indicative of said sample of thyroid tissue being benign or normal; and

(e) outputting said electronic report that is indicative of said sample of thyroid tissue being benign or normal.

2. The method of claim **1**, wherein said three or more gene expression products comprise four or more gene expression products, and wherein said at least three genes or corresponding Transcript Cluster ID Nos selected from AKT1, PIK3CA, PTEN, NTRK3 and ALK comprise at least four genes or corresponding Transcript Cluster ID Nos selected from AKT1, PIK3CA, PTEN, NTRK3 and ALK.

3. The method of claim **1**, further comprising assaying expression levels of BRAF, RET, RAS, CTNNB1, TSHR, PPARGC1A, MET, PTH, KRT7, CALCA, TP53, AKT1, PIK3CA, PTEN, NTRK3, ALK, EIF1AY, NTRK2, IGF2BP2, SLC5A8 and TTF1 in said sample of thyroid tissue obtained from said subject and wherein said at least three genes or corresponding Transcript Cluster ID Nos selected from AKT1, PIK3CA, PTEN, NTRK3 and ALK comprise BRAF, RET, RAS, CTNNB1, TSHR, PPARGC1A, MET, PTH, KRT7, CALCA, TP53, AKT1, PIK3CA, PTEN, NTRK3, ALK, EIF1AY, NTRK2, IGF2BP2, SLC5A8 and TTF1 or corresponding Transcript Cluster ID Nos.

4. The method of claim **1**, wherein said algorithm is trained with a training set comprising a training sample obtained by fine needle aspiration.

5. The method of claim **1**, wherein said algorithm is trained with a training set comprising a training sample obtained by fine needle aspiration and a training sample obtained by surgical biopsy.

6. The method of claim **1**, wherein said algorithm is trained with a training set comprising at least 200 training samples of thyroid tissue.

7. The method of claim **1**, wherein said algorithm is trained by correlating a gene expression profile of a first sub-type of thyroid tissue with a gene expression profile of at least six sub-types of thyroid tissue that are not of said first sub-type.

8. The method of claim **1**, wherein said algorithm is trained with a training set comprising a training sample with a pathology selected from the group consisting of: metastatic melanoma, metastatic renal carcinoma, metastatic breast carcinoma, and metastatic B cell lymphoma.

9. The method of claim **8**, wherein said pathology of said training sample is metastatic B cell lymphoma.

10. The method of claim **1**, wherein said sample of thyroid tissue has not previously received a definitive diagnosis.

11. The method of claim **1**, wherein said sample of thyroid tissue is subjected to cytological testing that indicates the sample is ambiguous or suspicious.

12. The method of claim **1**, wherein said sample of thyroid tissue is a formalin-fixed-paraffin-embedded sample.

13. The method of claim **1**, wherein said algorithm has a specificity greater than 70%.

14. The method of claim **1**, wherein said algorithm has a negative predictive value (NPV) of at least 95%.

15. The method of claim **1**, wherein said algorithm has an overall classification error rate of less than 6%.

16. The method of claim **1**, wherein said sample of thyroid tissue is obtained by needle aspiration, fine needle aspiration, core needle biopsy, vacuum assisted biopsy, large core biopsy, incisional biopsy, excisional biopsy, punch biopsy, shave biopsy, or skin biopsy.

17. The method of claim **1**, wherein said sample of thyroid tissue comprises thyroid cells and said sample of thyroid tissue is obtained by fine needle aspiration.

18. The method of claim **1**, wherein said gene expression products comprise RNA expression products.

19. The method of claim **18**, wherein a level of said RNA expression products is measured by microarray, SAGE, blotting, RT-PCR, quantitative PCR, or sequencing.

20. The method of claim **1**, wherein said algorithm is trained with at least three training samples, each of which exhibits a different malignant pathology.

21. The method of claim **20**, wherein each of said at least three training samples is obtained from a different tissue type and wherein said different tissue type is selected from the following tissue types: follicular carcinoma, lymphocytic thyroiditis, follicular variant papillary thyroid carcinoma, papillary thyroid carcinoma, nodular hyperplasia, medullary thyroid carcinoma, Hurthle cell carcinoma, Hurthle cell adenoma, anaplastic thyroid carcinoma, metastatic melanoma, metastatic renal carcinoma, metastatic breast carcinoma, parathyroid, and metastatic B cell lymphoma.

22. The method of claim **1**, wherein said electronic report is sent to a party via a communication medium.

23. The method of claim **1**, wherein said electronic report is presented on a computer screen.

24. The method of claim **1**, wherein said electronic report is presented as a paper record.

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