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(54) METHODS AND KITS FOR DIAGNOSIS AND TRIAGE OF PATIENTS WITH COLORECTAL LIVER METASTASES

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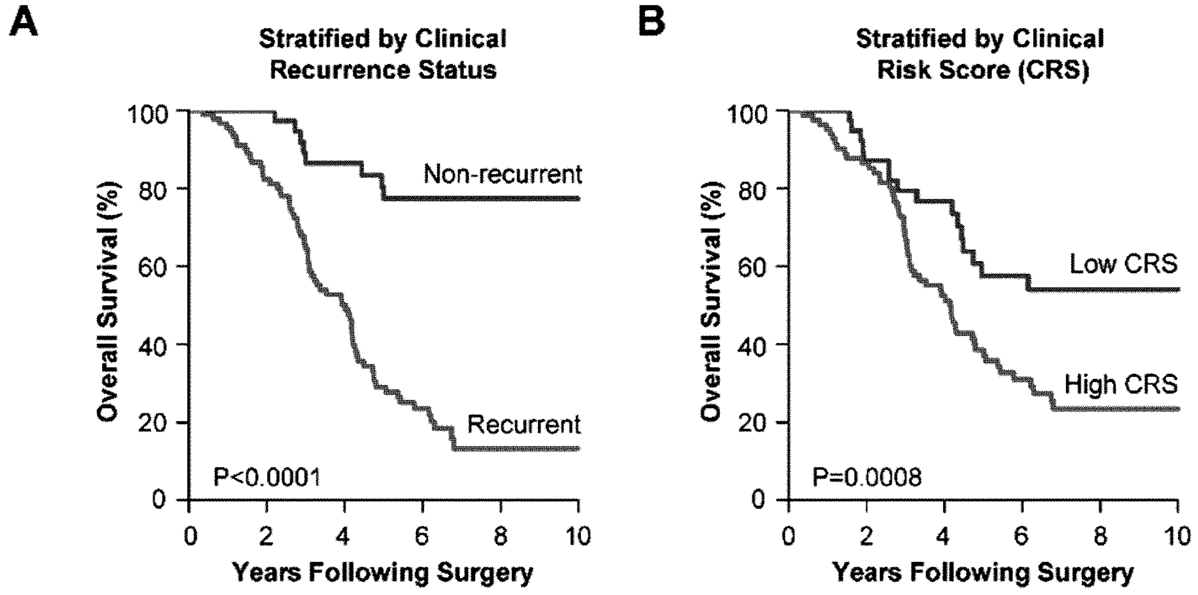
CPC *C12Q 1/6886* (2013.01); *C12Q 2600/178* (2013.01)

(57) ABSTRACT

Methods, assays, and compositions for identifying molecular subtypes of metastatic cancer are disclosed. Methods include determining expression levels of genes and/or miRNAs in a sample of metastatic tissue and identifying the molecular subtype of the metastasis based on the determined expression levels. Methods may further include providing a prognosis and making treatment decision based on the molecular subtype of the metastasis.



No. at risk						
Non-recurrent	43	38	31	24	19	13
Recurrent	91	75	39	15	6	4

No. at risk						
Low CRS	43	35	25	18	11	7
High CRS	82	70	40	18	13	10

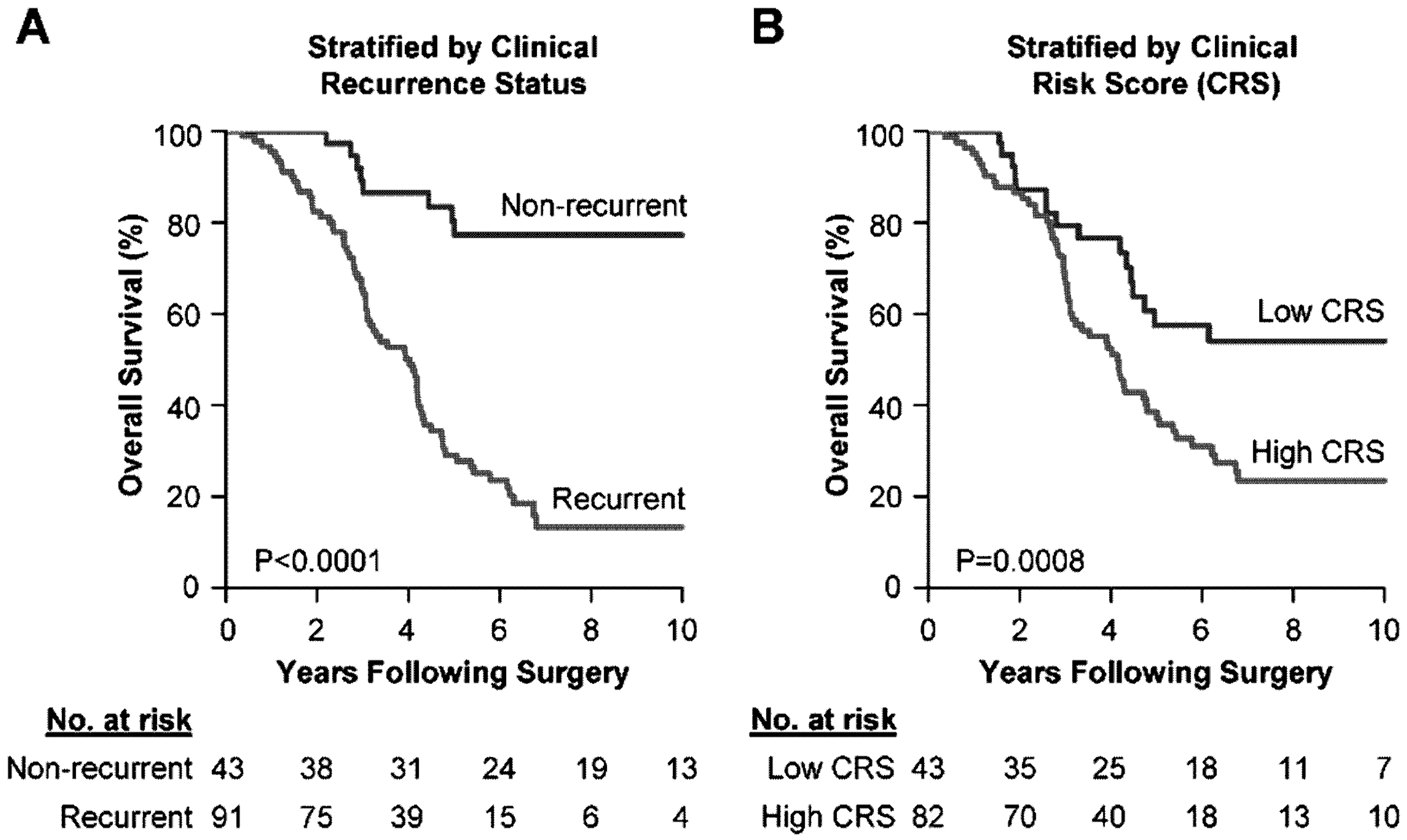

A
Stratified by Clinical Recurrence Status
Overall Survival (%)
100
80
60
40
20
0
Non-recurrent
Recurrent
P<0.0001
0
2
4
6
8
10
Years Following Surgery
No. at risk
Non-recurrent 43 38 31 24 19 13
Recurrent 91 75 39 15 6 4
B
Stratified by Clinical Risk Score (CRS)
Overall Survival (%)
100
80
60
40
20
0
Low CRS
High CRS
P=0.0008
0
2
4
6
8
10
Years Following Surgery
No. at risk
Low CRS 43 35 25 18 11 7
High CRS 82 70 40 18 13 10

FIG. 1A-B

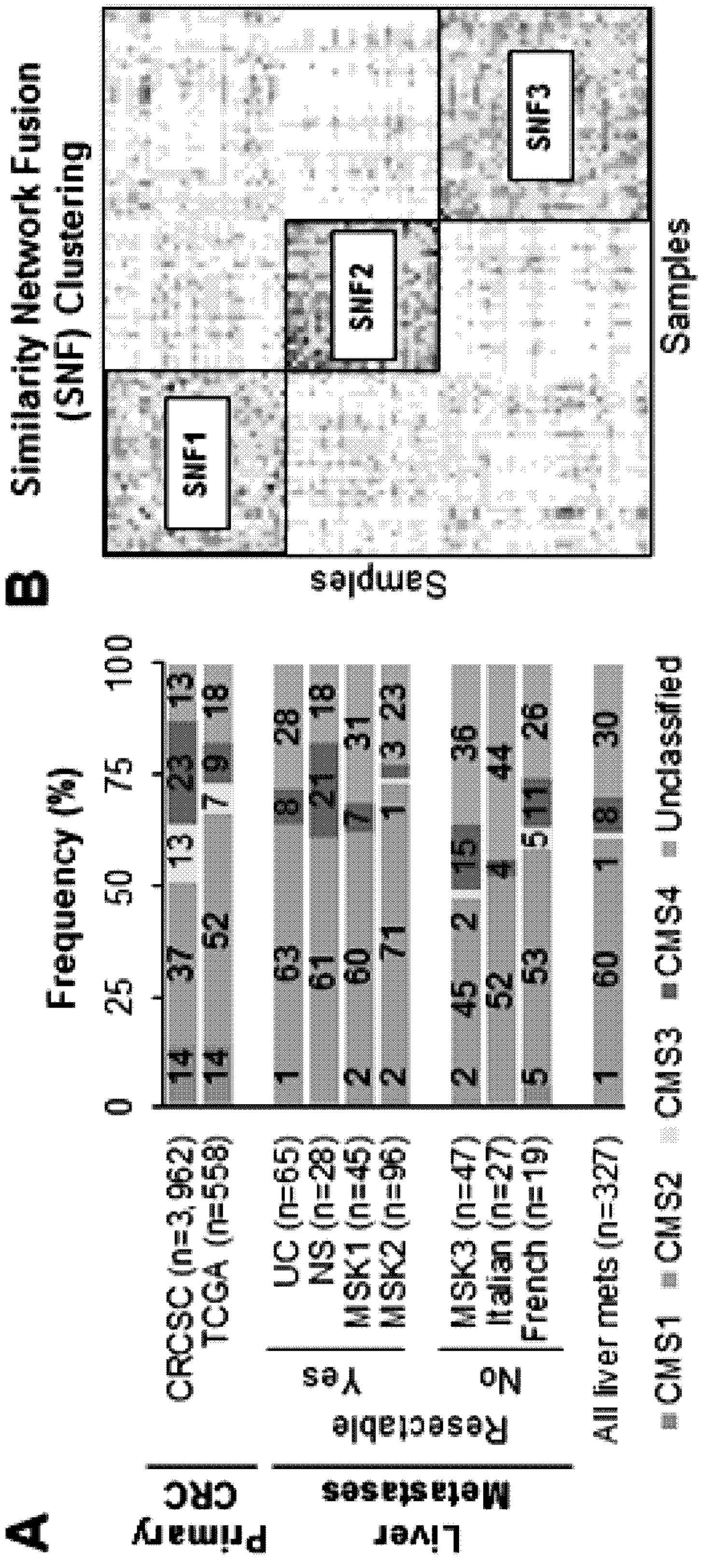

A
Primary CRC
Liver Metastases
Resectable
Yes
No
CRCSC (n=3,962)
TCGA (n=558)
UC (n=65)
NS (n=28)
MSK1 (n=45)
MSK2 (n=96)
MSK3 (n=47)
Italian (n=27)
French (n=19)
All liver mets (n=327)
Frequency (%)
0
25
50
75
100
14 37 13 23 13
14 52 7 9 18
1 63 8 28
61 21 18
2 60 7 31
2 71 1 3 23
2 45 2 15 36
52 4 44
5 53 5 11 26
1 60 1 8 30
CMS1
CMS2
CMS3
CMS4
Unclassified
B
Similarity Network Fusion (SNF) Clustering
SNF1
SNF2
SNF3
Samples
Samples

FIG. 2A-B

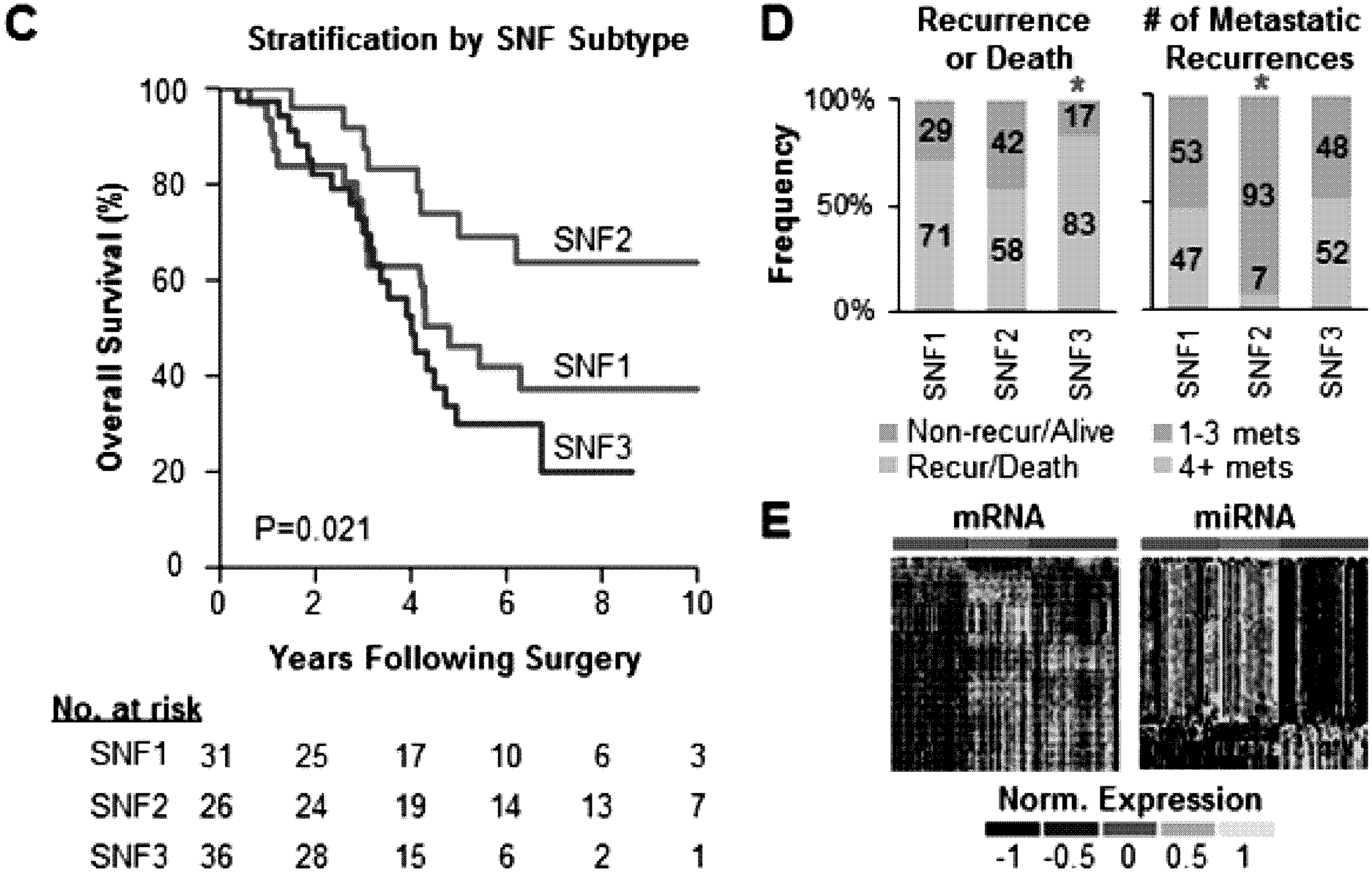

C
Stratification by SNF Subtype
Overall Survival (%)
100
80
60
40
20
0
0
2
4
6
8
10
Years Following Surgery
SNF2
SNF1
SNF3
P=0.021
No. at risk
SNF1 31 25 17 10 6 3
SNF2 26 24 19 14 13 7
SNF3 36 28 15 6 2 1
D
Recurrence or Death
# of Metastatic Recurrences
Frequency
100%
50%
0%
29
71
42
58
17
83
*
53
47
93
7
48
52
*
SNF1
SNF2
SNF3
SNF1
SNF2
SNF3
Non-recur/Alive
Recur/Death
1-3 mets
4+ mets
E
mRNA
miRNA
Norm. Expression
-1
-0.5
0
0.5
1

FIG. 2C-E

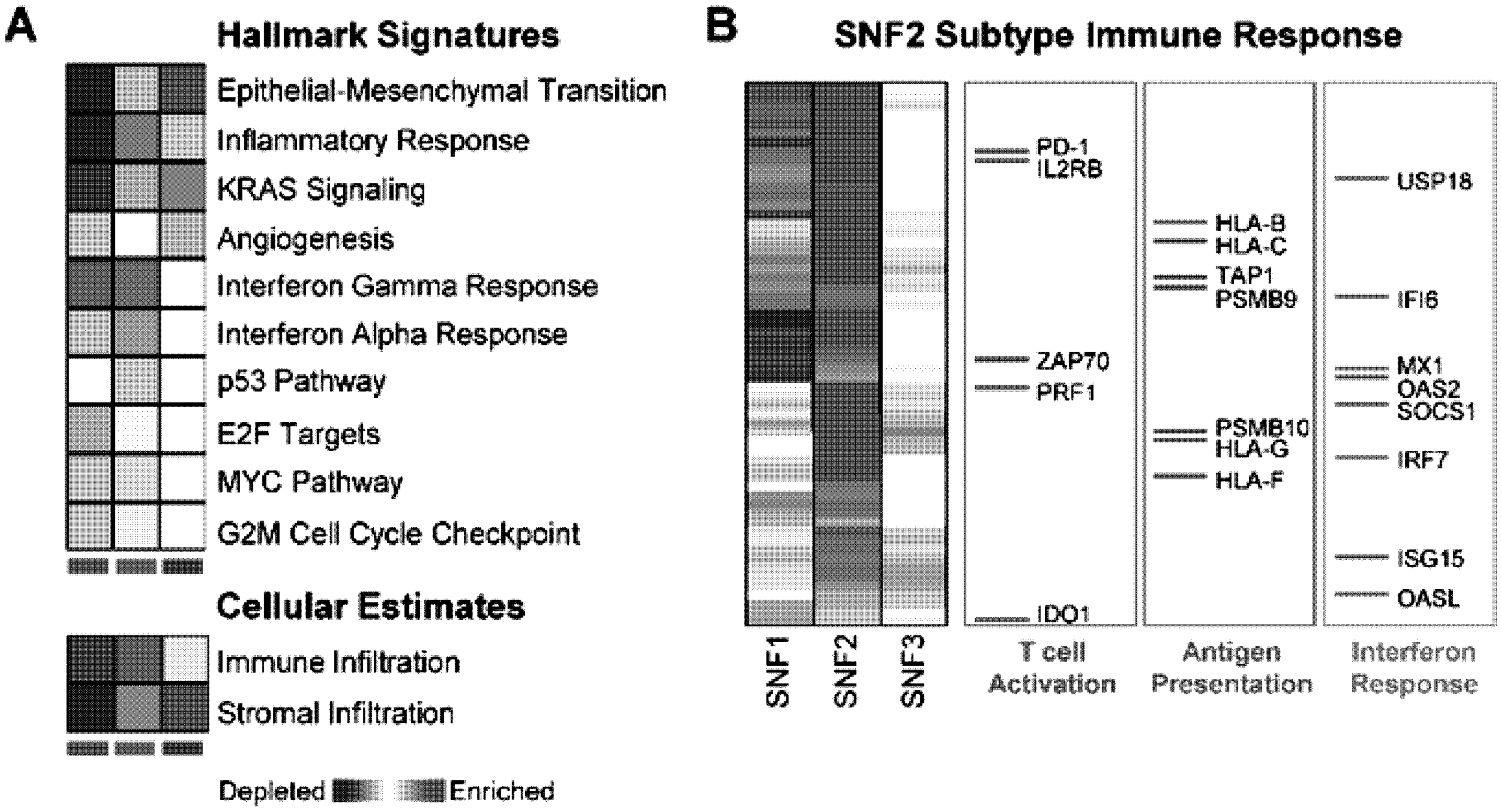

A
Hallmark Signatures
Epithelial-Mesenchymal Transition
Inflammatory Response
KRAS Signaling
Angiogenesis
Interferon Gamma Response
Interferon Alpha Response
p53 Pathway
E2F Targets
MYC Pathway
G2M Cell Cycle Checkpoint
Cellular Estimates
Immune Infiltration
Stromal Infiltration
Depleted
Enriched
B
SNF2 Subtype Immune Response
SNF1
SNF2
SNF3
PD-1
IL2RB
ZAP70
PRF1
IDO1
T cell Activation
HLA-B
HLA-C
TAP1
PSMB9
PSMB10
HLA-G
HLA-F
Antigen Presentation
USP18
IFI6
MX1
OAS2
SOCS1
IRF7
ISG15
OASL
Interferon Response

FIG. 3A-B

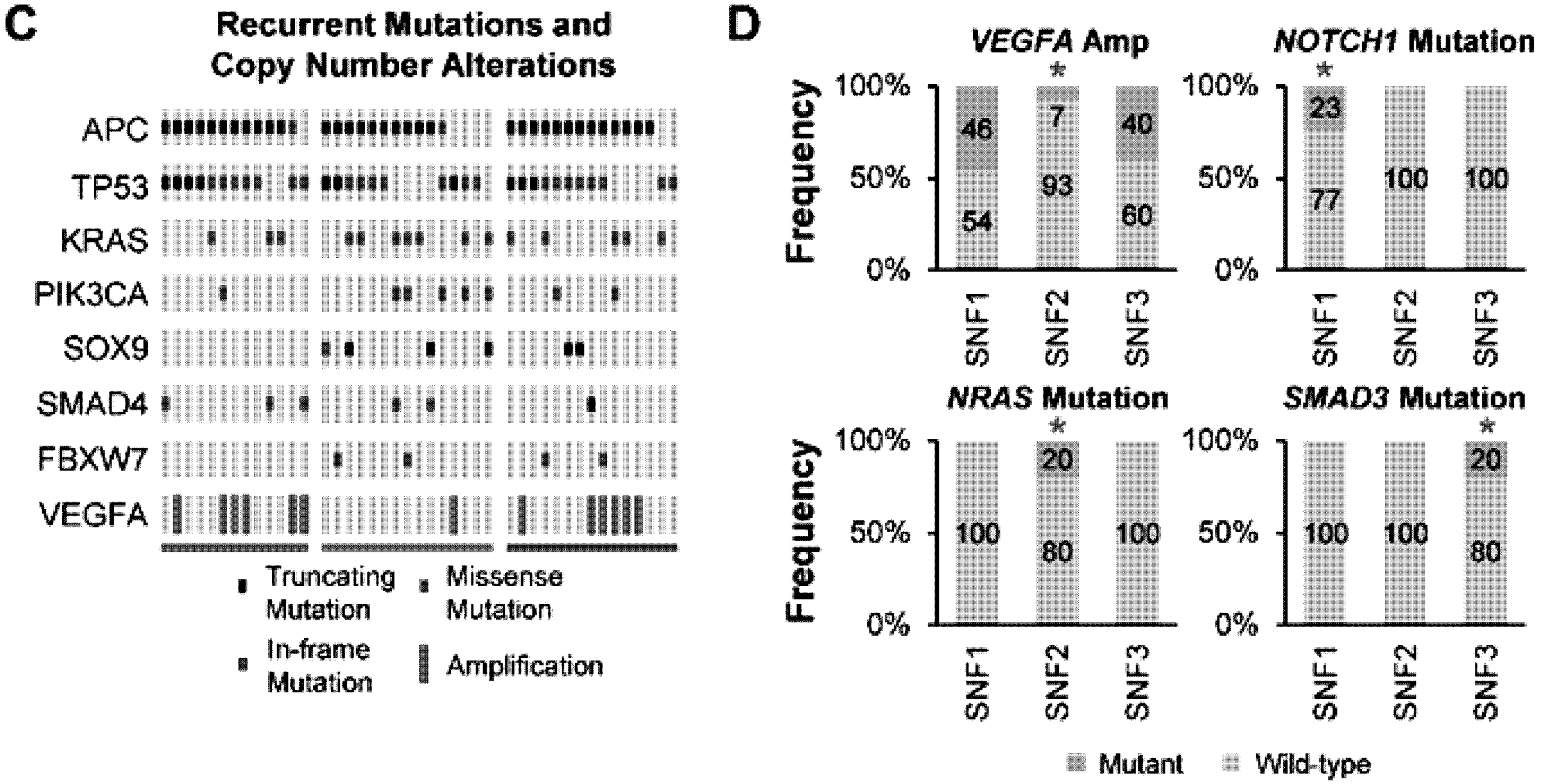

C
Recurrent Mutations and Copy Number Alterations
APC
TP53
KRAS
PIK3CA
SOX9
SMAD4
FBXW7
VEGFA
Truncating Mutation
Missense Mutation
In-frame Mutation
Amplification
D
VEGFA Amp
NOTCH1 Mutation
NRAS Mutation
SMAD3 Mutation
Frequency
100%
50%
0%
SNF1
SNF2
SNF3
*
46
54
7
93
40
60
23
77
100
100
20
80
100
100
100
20
80
Mutant
Wild-type

FIG. 3C-D

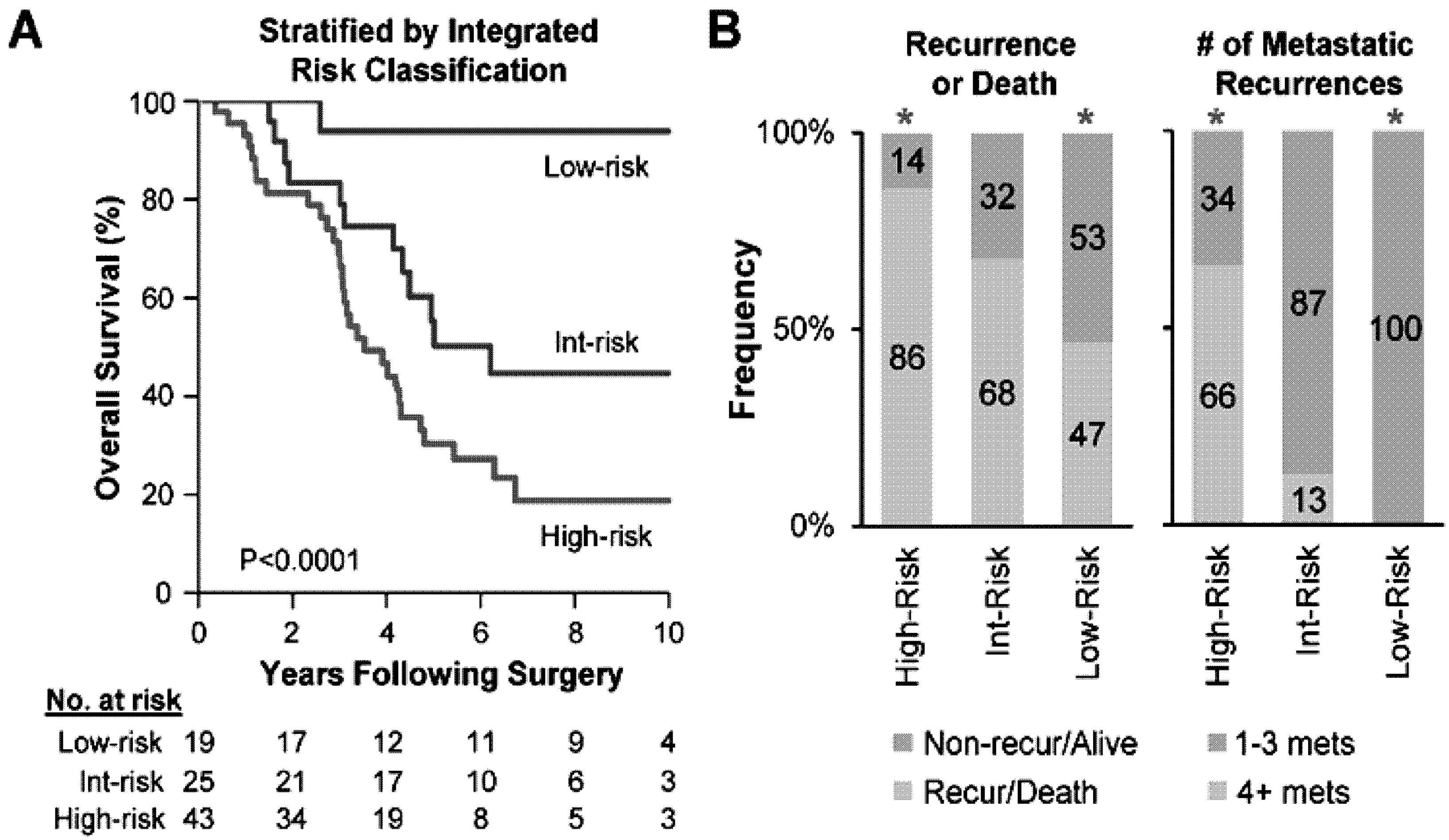

A
Stratified by Integrated Risk Classification
Overall Survival (%)
100
80
60
40
20
0
0
2
4
6
8
10
Years Following Surgery
Low-risk
Int-risk
High-risk
P<0.0001
No. at risk
Low-risk 19 17 12 11 9 4
Int-risk 25 21 17 10 6 3
High-risk 43 34 19 8 5 3
B
Recurrence or Death
# of Metastatic Recurrences
Frequency
100%
50%
0%
*
14
86
32
68
53
47
34
66
87
13
100
High-Risk
Int-Risk
Low-Risk
▨ Non-recur/Alive
▨ Recur/Death
▨ 1-3 mets
▨ 4+ mets

FIG. 4A-B

	SNF1 Canonical	**SNF2 Immune**	**SNF3 Stromal**
Frequency	33%	28%	39%
Molecular signatures	↓immune and stroma E2F/MYC signaling DNA damage and cell cycle	↑immune Interferon signaling p53 pathway	↑stroma KRAS signaling EMT and angiogenesis
Specific Mutations	*NOTCH1* and *PIK3C2B*	*NRAS*, *CDK12*, and *EBF1*	*SMAD3*
Metastatic Recurrences	Many	Few	Many
Overall Survival	Intermediate	Favorable	Unfavorable

FIG. 4C

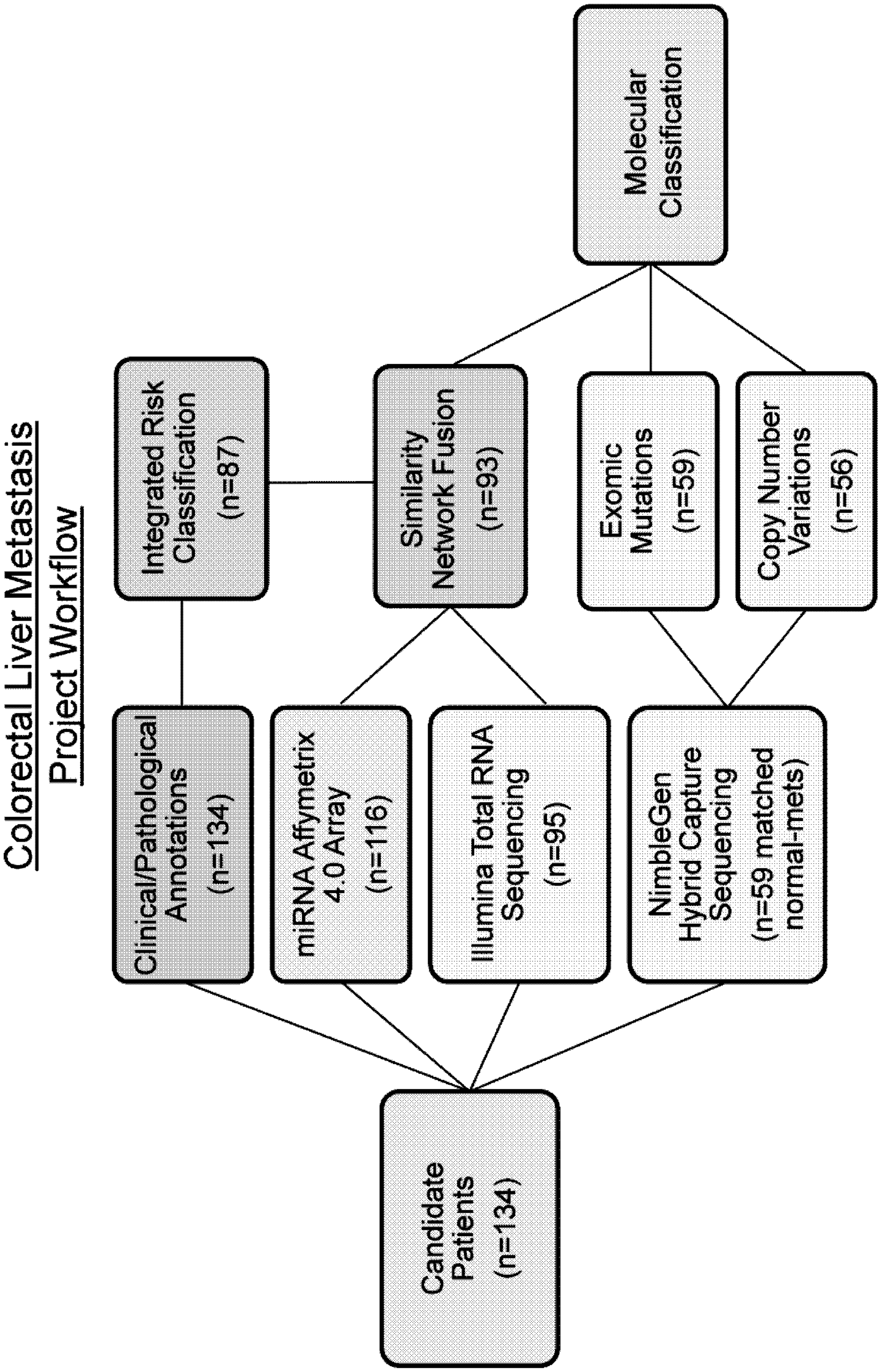
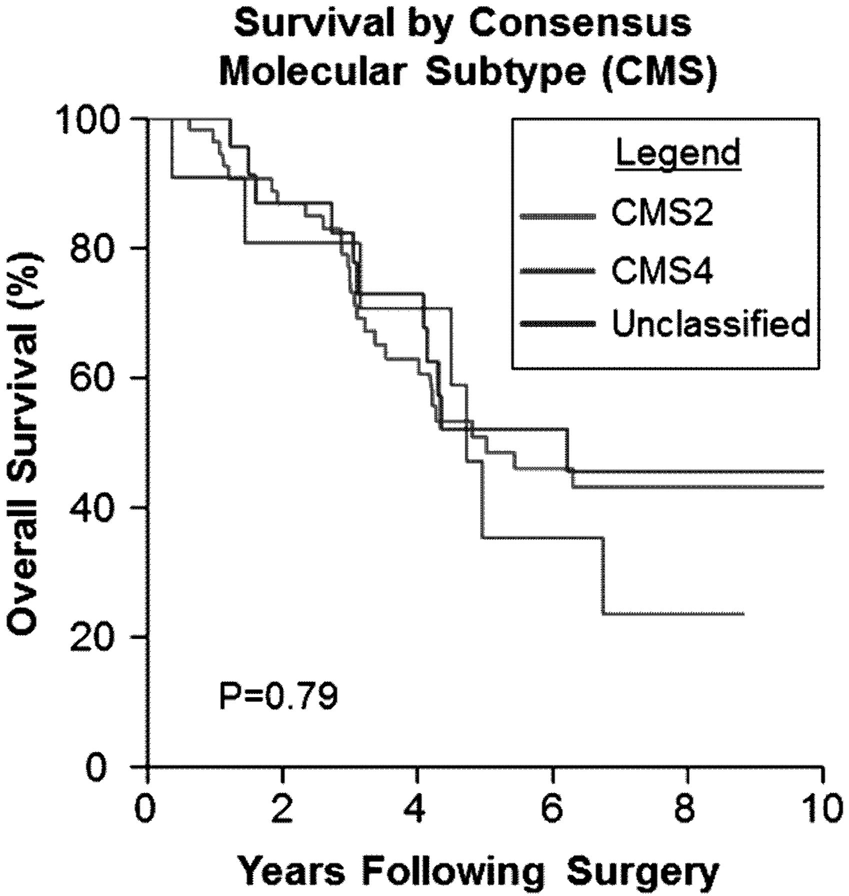

Colorectal Liver Metastasis
Project Workflow
Candidate Patients (n=134)
Clinical/Pathological Annotations (n=134)
miRNA Affymetrix 4.0 Array (n=116)
Illumina Total RNA Sequencing (n=95)
NimbleGen Hybrid Capture Sequencing (n=59 matched normal-mets)
Integrated Risk Classification (n=87)
Similarity Network Fusion (n=93)
Exomic Mutations (n=59)
Copy Number Variations (n=56)
Molecular Classification

FIG. 5



No. at risk						
CMS2	58	46	28	17	14	9
CMS4	11	9	8	4	3	1
Unclassified	23	20	15	9	6	2

FIG. 6

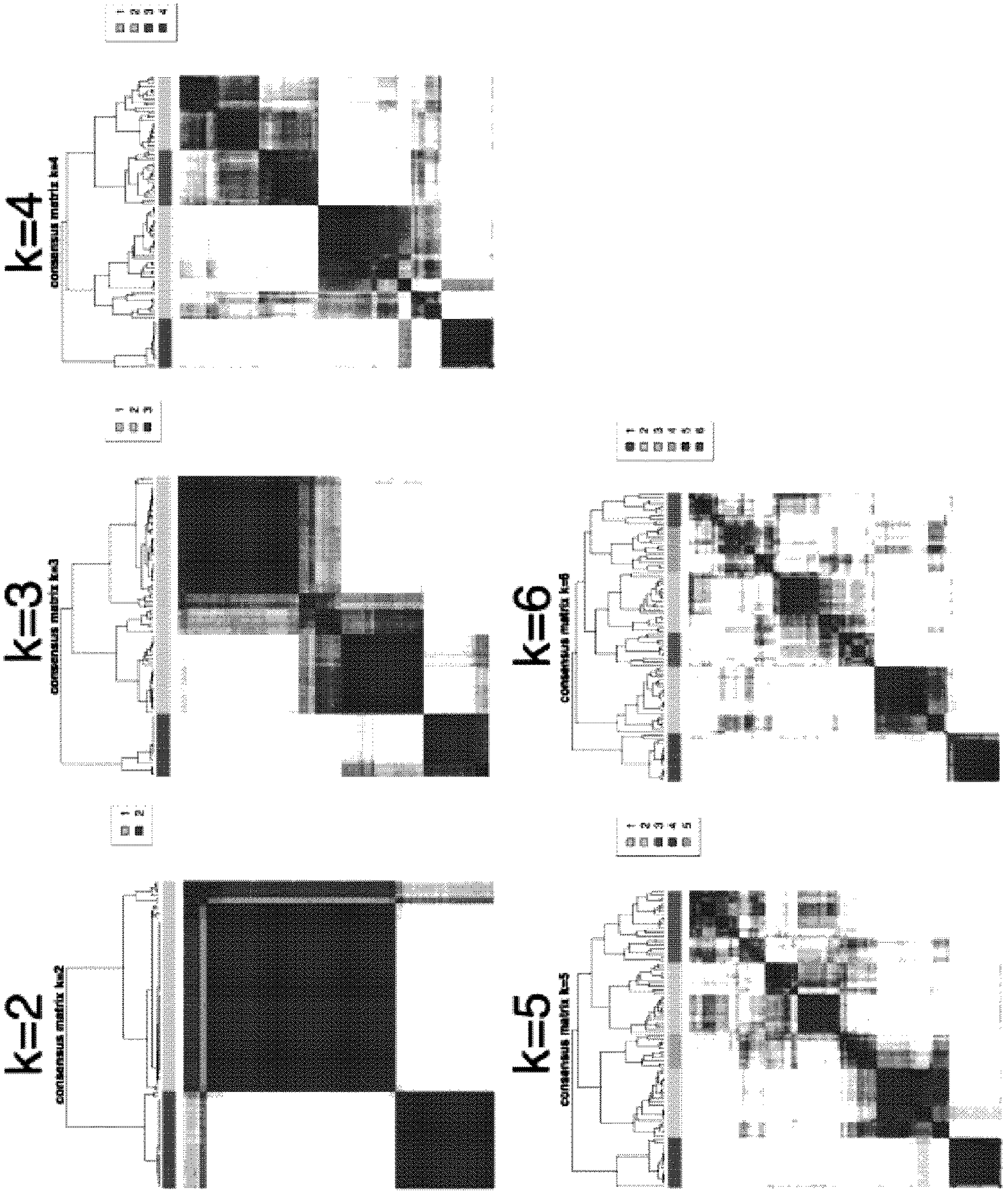

k=2
consensus matrix k=2
1
2
k=3
consensus matrix k=3
1
2
3
k=4
consensus matrix k=4
1
2
3
4
k=5
consensus matrix k=5
1
2
3
4
5
k=6
consensus matrix k=6
1
2
3
4
5
6

FIG. 7A

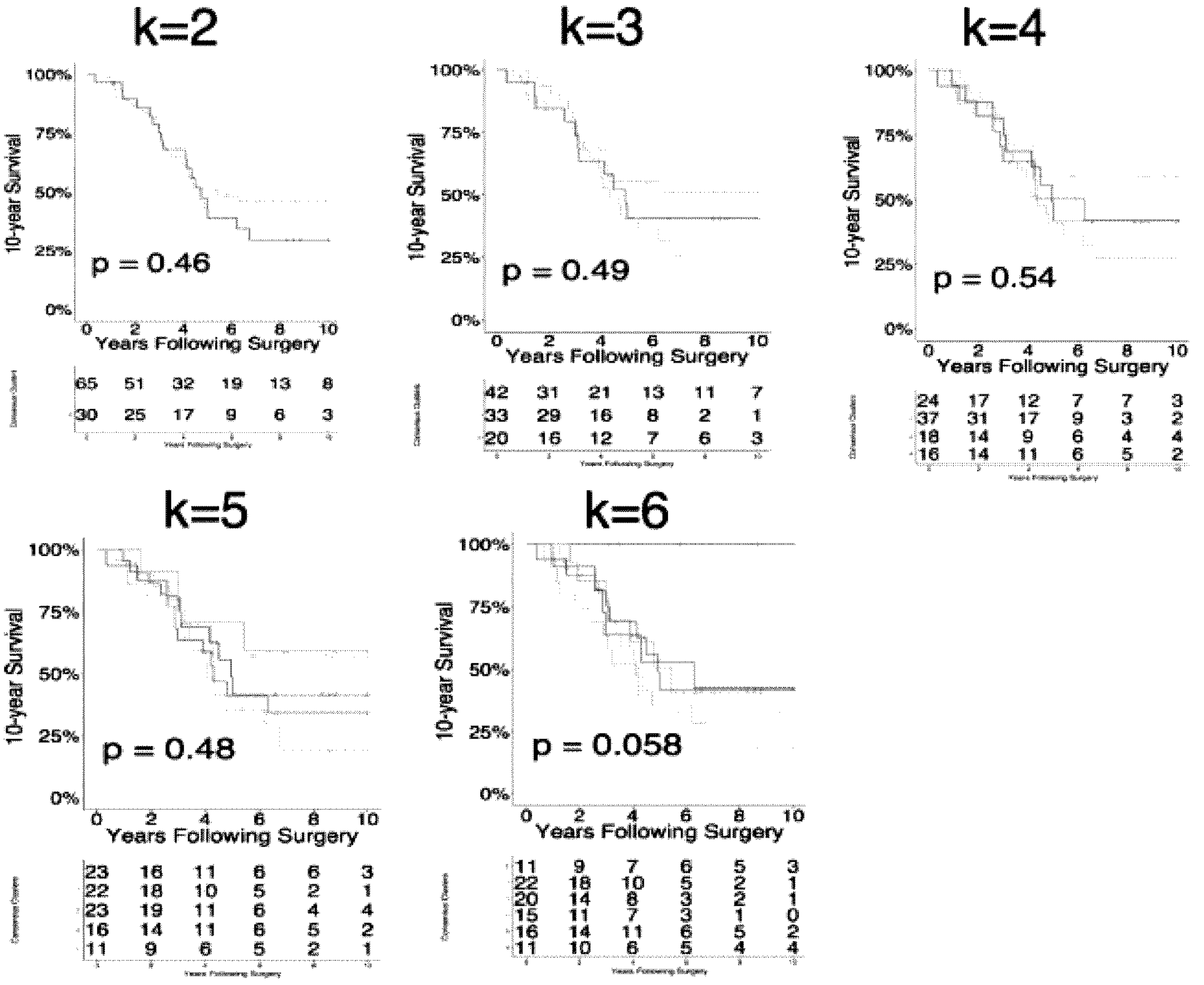

k=2
100%
75%
50%
25%
0%
10-year Survival
p = 0.46
0 2 4 6 8 10
Years Following Surgery
65 51 32 19 13 8
30 25 17 9 6 3
k=3
100%
75%
50%
25%
0%
10-year Survival
p = 0.49
0 2 4 6 8 10
Years Following Surgery
42 31 21 13 11 7
33 29 16 8 2 1
20 16 12 7 6 3
k=4
100%
75%
50%
25%
0%
10-year Survival
p = 0.54
0 2 4 6 8 10
Years Following Surgery
24 17 12 7 7 3
37 31 17 9 3 2
18 14 9 6 4 4
16 14 11 6 5 2
k=5
100%
75%
50%
25%
0%
10-year Survival
p = 0.48
0 2 4 6 8 10
Years Following Surgery
23 16 11 6 6 3
22 18 10 5 2 1
23 19 11 6 4 4
16 14 11 6 5 2
11 9 6 5 2 1
k=6
100%
75%
50%
25%
0%
10-year Survival
p = 0.058
0 2 4 6 8 10
Years Following Surgery
11 9 7 6 5 3
22 18 10 5 2 1
20 14 8 3 2 1
15 11 7 3 1 0
16 14 11 6 5 2
11 10 6 5 4 4

FIG. 7B

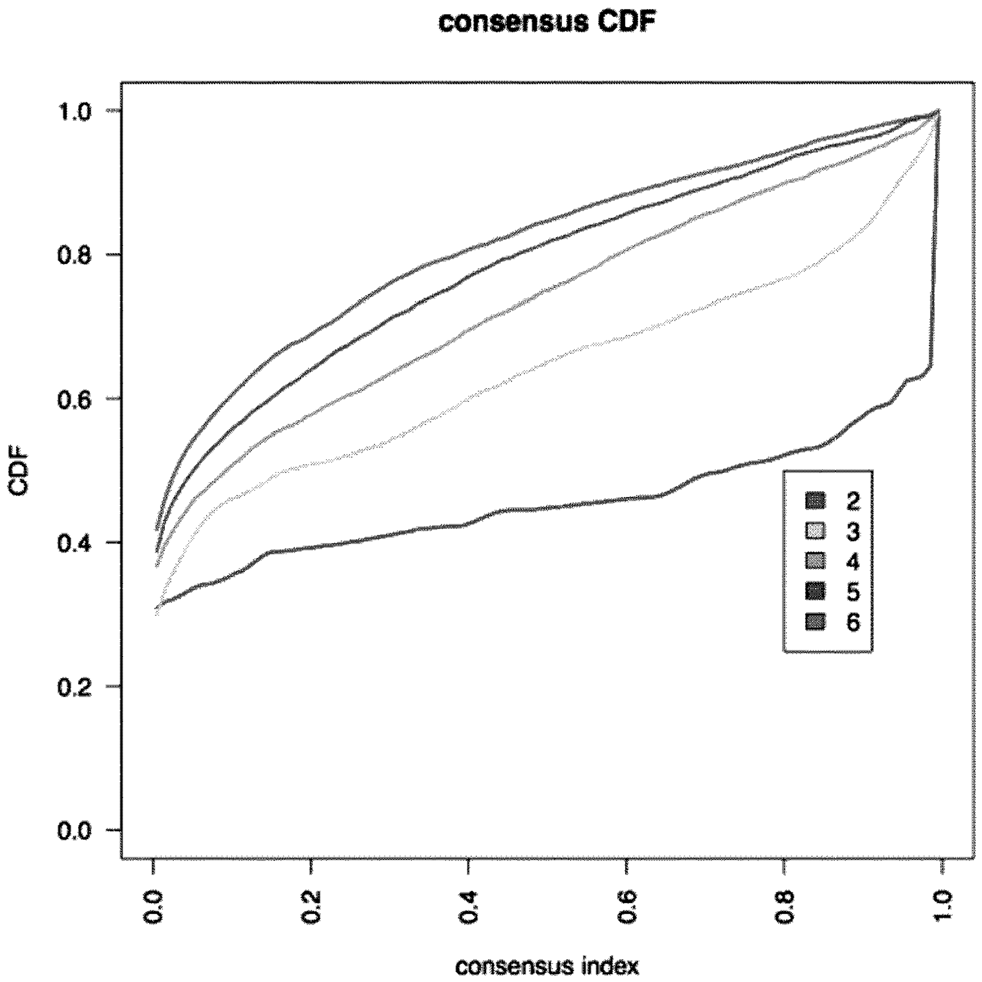

consensus CDF
1.0
0.8
0.6
0.4
0.2
0.0
CDF
0.0
0.2
0.4
0.6
0.8
1.0
consensus index
▨ 2
▨ 3
▨ 4
▨ 5
▨ 6

FIG. 7C

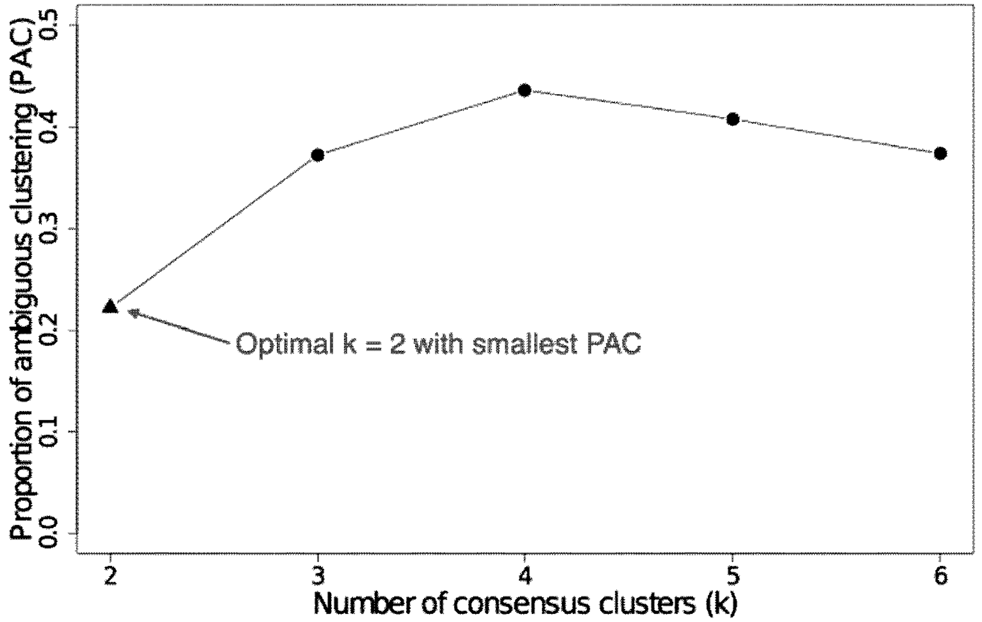

Proportion of ambiguous clustering (PAC)
0.0
0.1
0.2
0.3
0.4
0.5
2
3
4
5
6
Number of consensus clusters (k)
Optimal k = 2 with smallest PAC

FIG. 7D

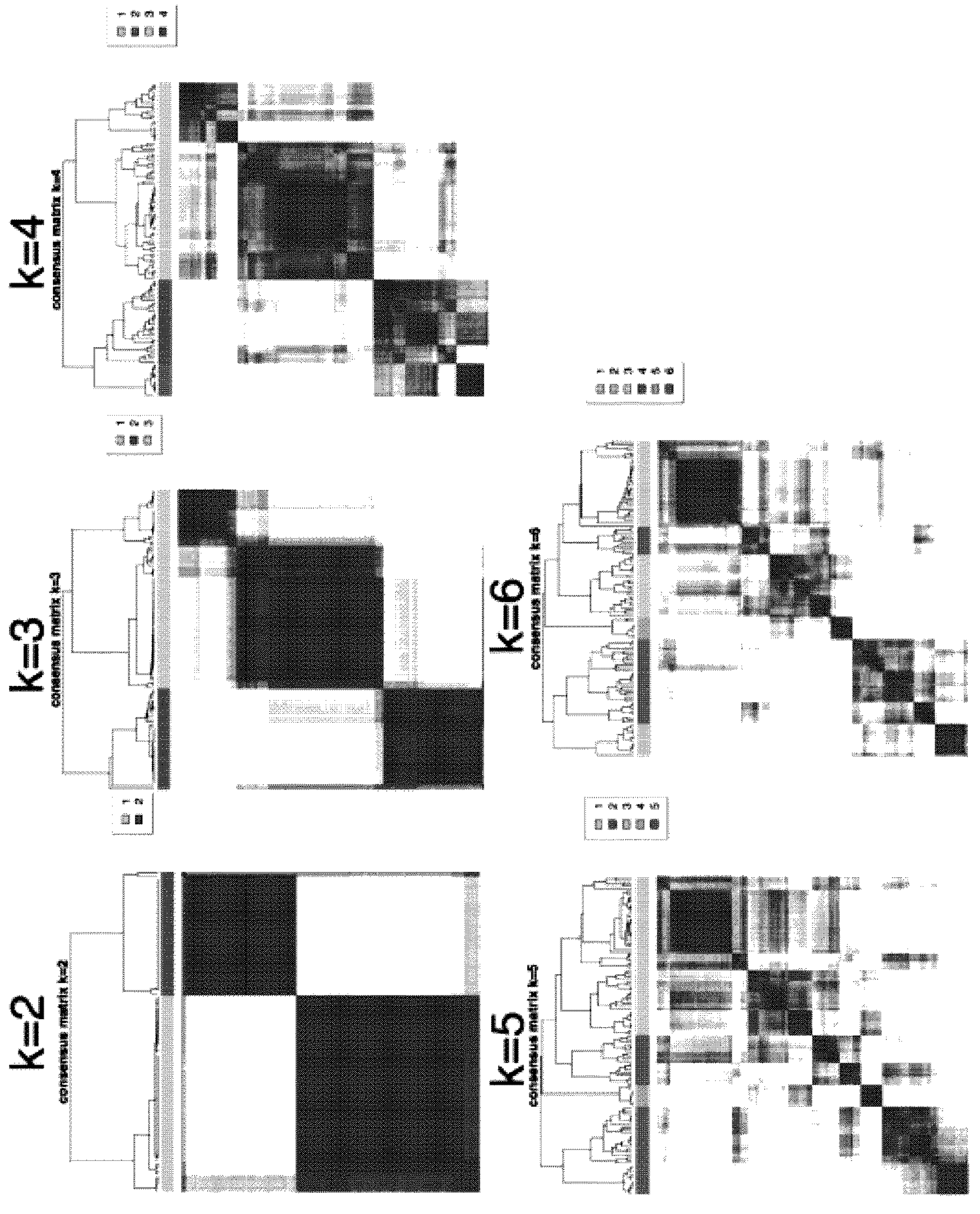

k=2
consensus matrix k=2
1
2
k=3
consensus matrix k=3
1
2
3
k=4
consensus matrix k=4
1
2
3
4
k=5
consensus matrix k=5
1
2
3
4
5
k=6
consensus matrix k=6
1
2
3
4
5
6

FIG. 8A

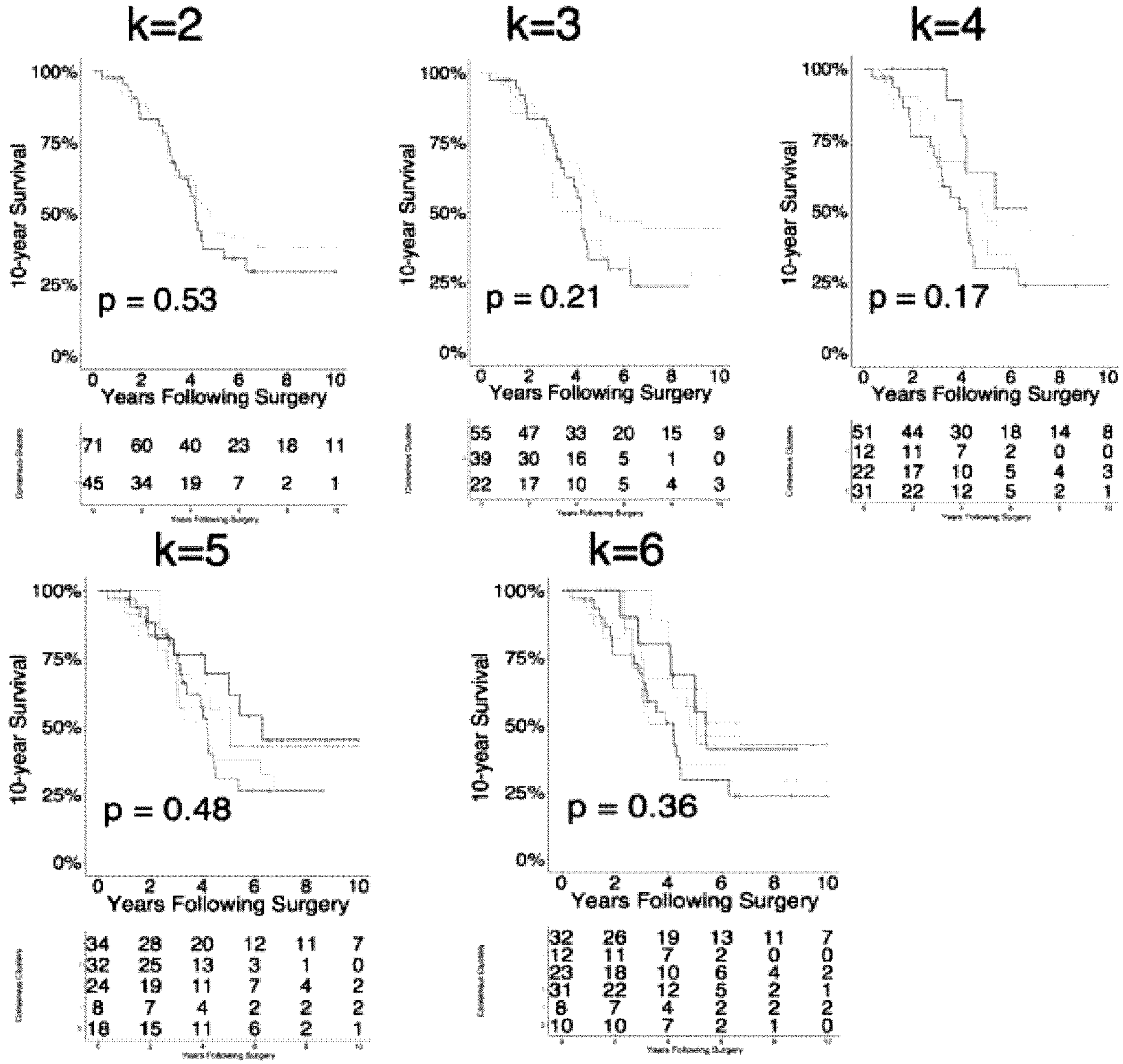

k=2
10-year Survival
100%
75%
50%
25%
0%
p = 0.53
0 2 4 6 8 10
Years Following Surgery
71 60 40 23 18 11
45 34 19 7 2 1
k=3
10-year Survival
100%
75%
50%
25%
0%
p = 0.21
0 2 4 6 8 10
Years Following Surgery
55 47 33 20 15 9
39 30 16 5 1 0
22 17 10 5 4 3
k=4
10-year Survival
100%
75%
50%
25%
0%
p = 0.17
0 2 4 6 8 10
Years Following Surgery
51 44 30 18 14 8
12 11 7 2 0 0
22 17 10 5 4 3
31 22 12 5 2 1
k=5
10-year Survival
100%
75%
50%
25%
0%
p = 0.48
0 2 4 6 8 10
Years Following Surgery
34 28 20 12 11 7
32 25 13 3 1 0
24 19 11 7 4 2
8 7 4 2 2 2
18 15 11 6 2 1
k=6
10-year Survival
100%
75%
50%
25%
0%
p = 0.36
0 2 4 6 8 10
Years Following Surgery
32 26 19 13 11 7
12 11 7 2 0 0
23 18 10 6 4 2
31 22 12 5 2 1
8 7 4 2 2 2
10 10 7 2 1 0

FIG. 8B

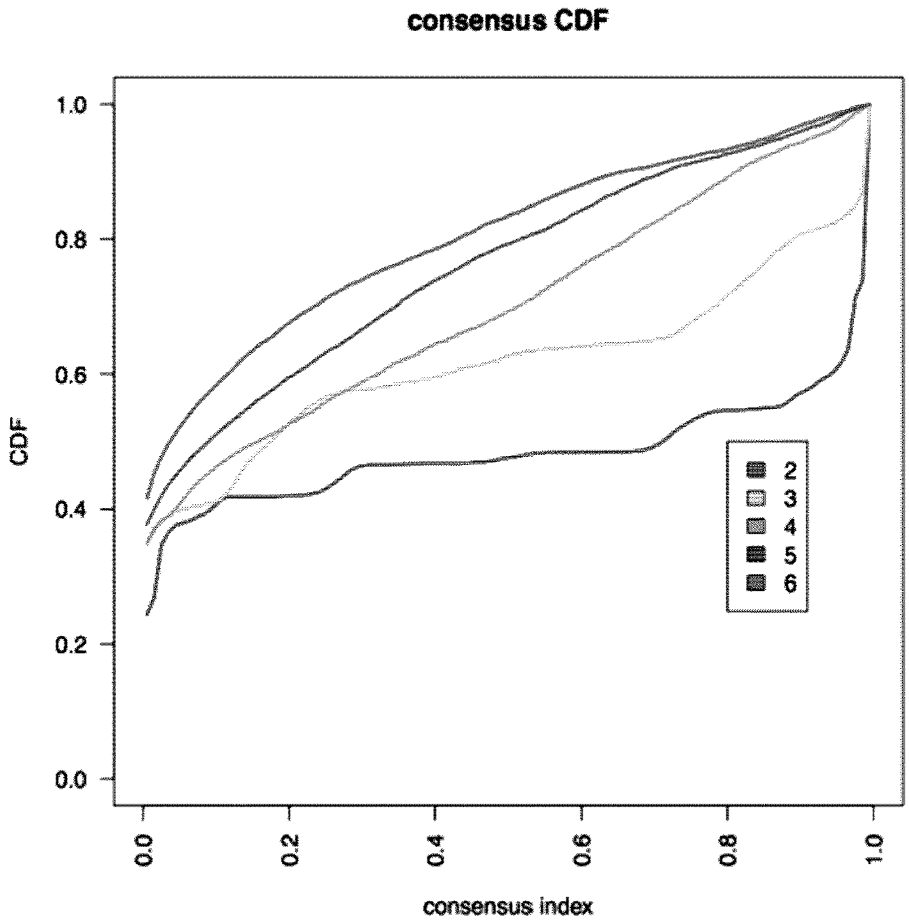

consensus CDF
1.0
0.8
0.6
0.4
0.2
0.0
CDF
2
3
4
5
6
0.0
0.2
0.4
0.6
0.8
1.0
consensus index

FIG. 8C

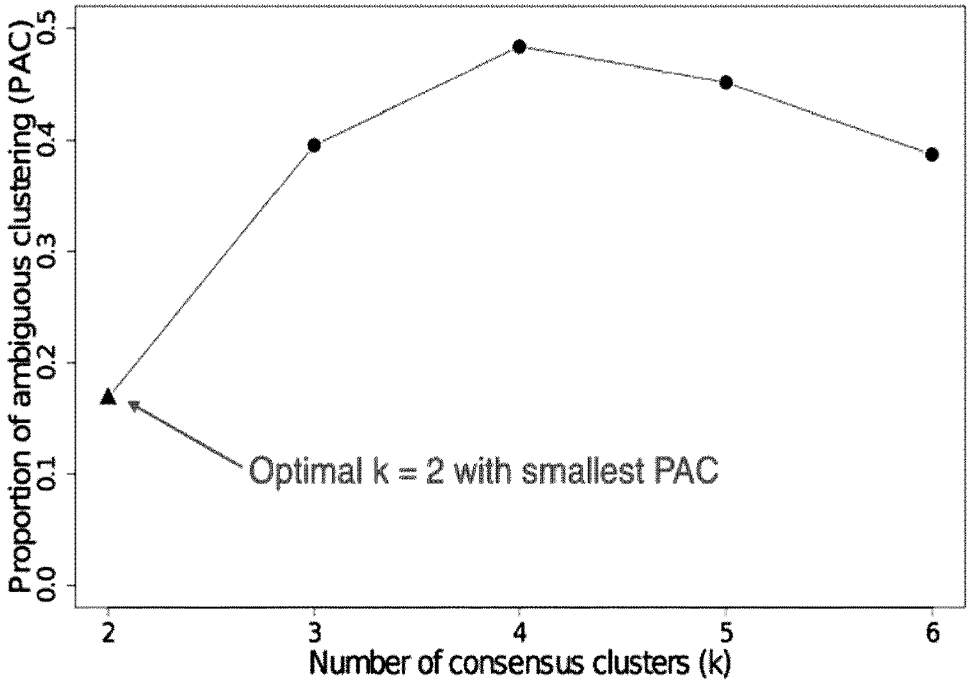

Proportion of ambiguous clustering (PAC)
0.0
0.1
0.2
0.3
0.4
0.5
Optimal k = 2 with smallest PAC
2
3
4
5
6
Number of consensus clusters (k)

FIG. 8D

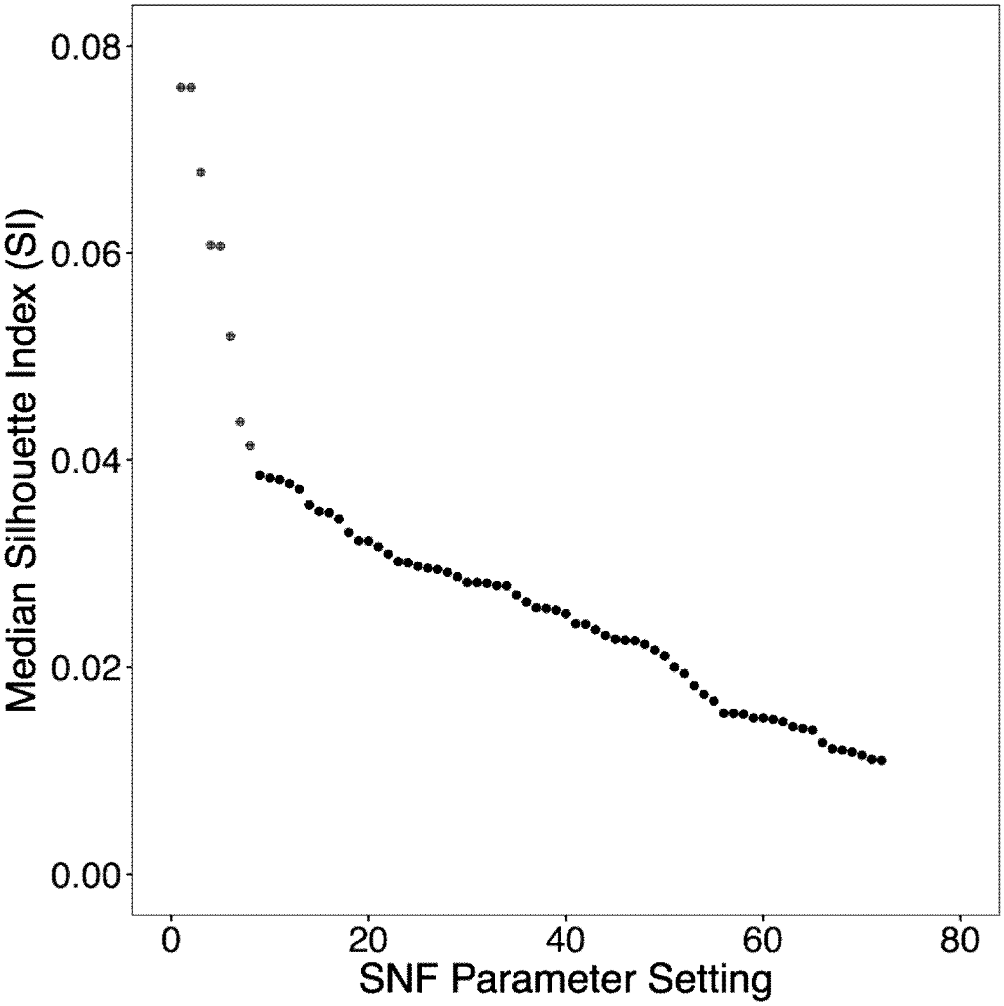

Median Silhouette Index (SI)
0.08
0.06
0.04
0.02
0.00
0
20
40
60
80
SNF Parameter Setting

FIG. 9

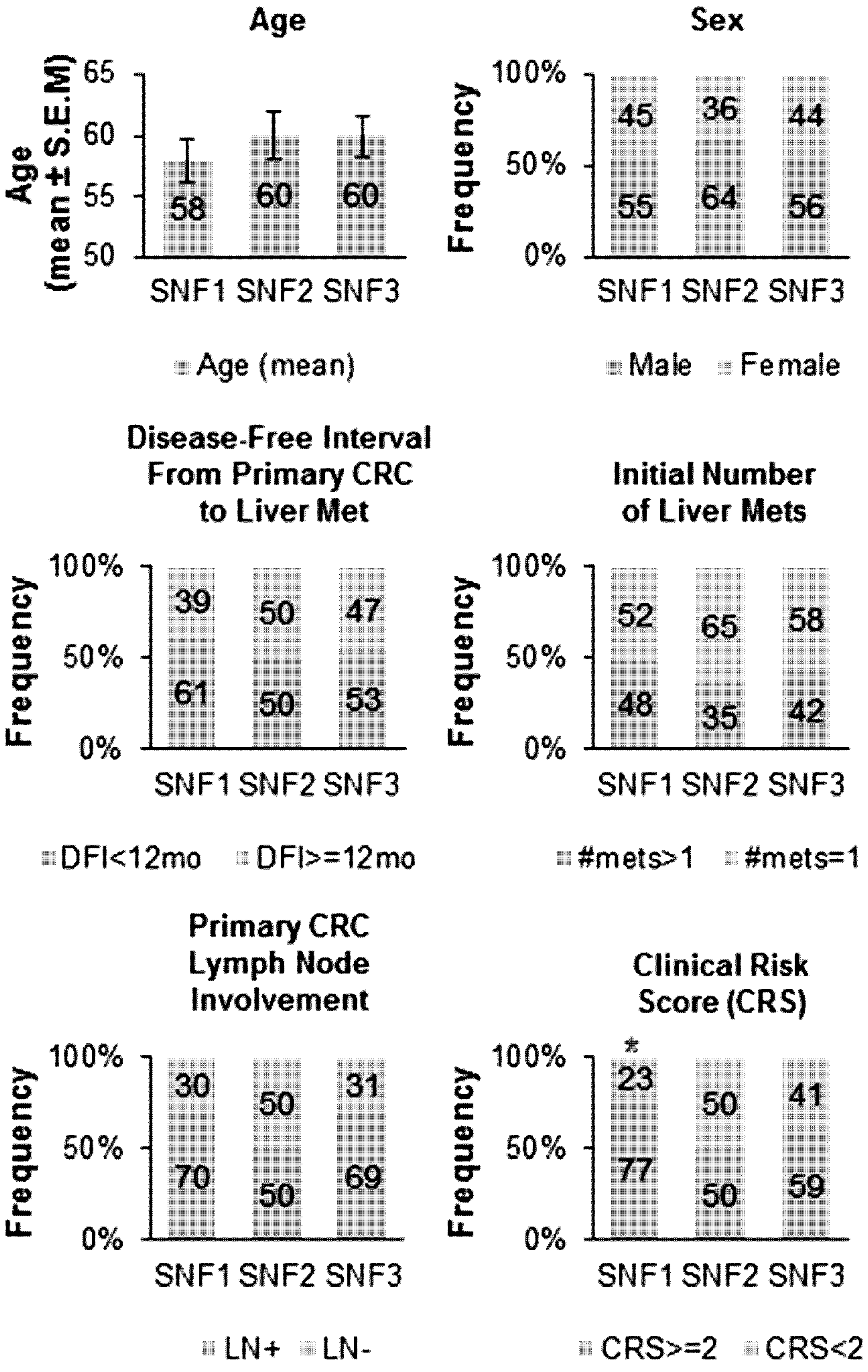

Age
Age (mean ± S.E.M)
65
60
55
50
58
60
60
SNF1 SNF2 SNF3
Age (mean)
Sex
Frequency
100%
50%
0%
45
36
44
55
64
56
SNF1 SNF2 SNF3
Male
Female
Disease-Free Interval From Primary CRC to Liver Met
Frequency
100%
50%
0%
39
50
47
61
50
53
SNF1 SNF2 SNF3
DFI<12mo
DFI>=12mo
Initial Number of Liver Mets
Frequency
100%
50%
0%
52
65
58
48
35
42
SNF1 SNF2 SNF3
#mets>1
#mets=1
Primary CRC Lymph Node Involvement
Frequency
100%
50%
0%
30
50
31
70
50
69
SNF1 SNF2 SNF3
LN+
LN-
Clinical Risk Score (CRS)
Frequency
100%
50%
0%
*
23
50
41
77
50
59
SNF1 SNF2 SNF3
CRS>=2
CRS<2

FIG. 10A

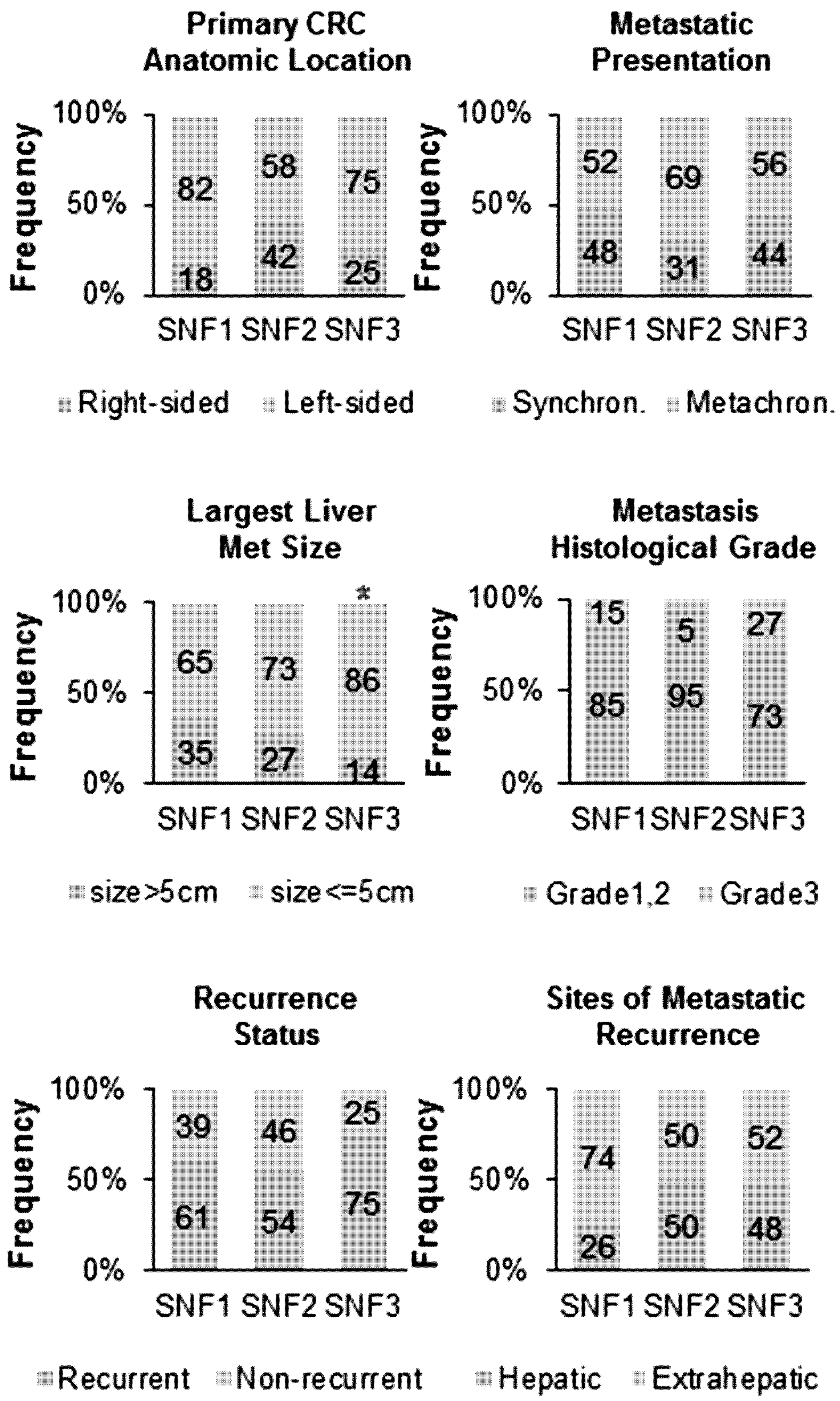
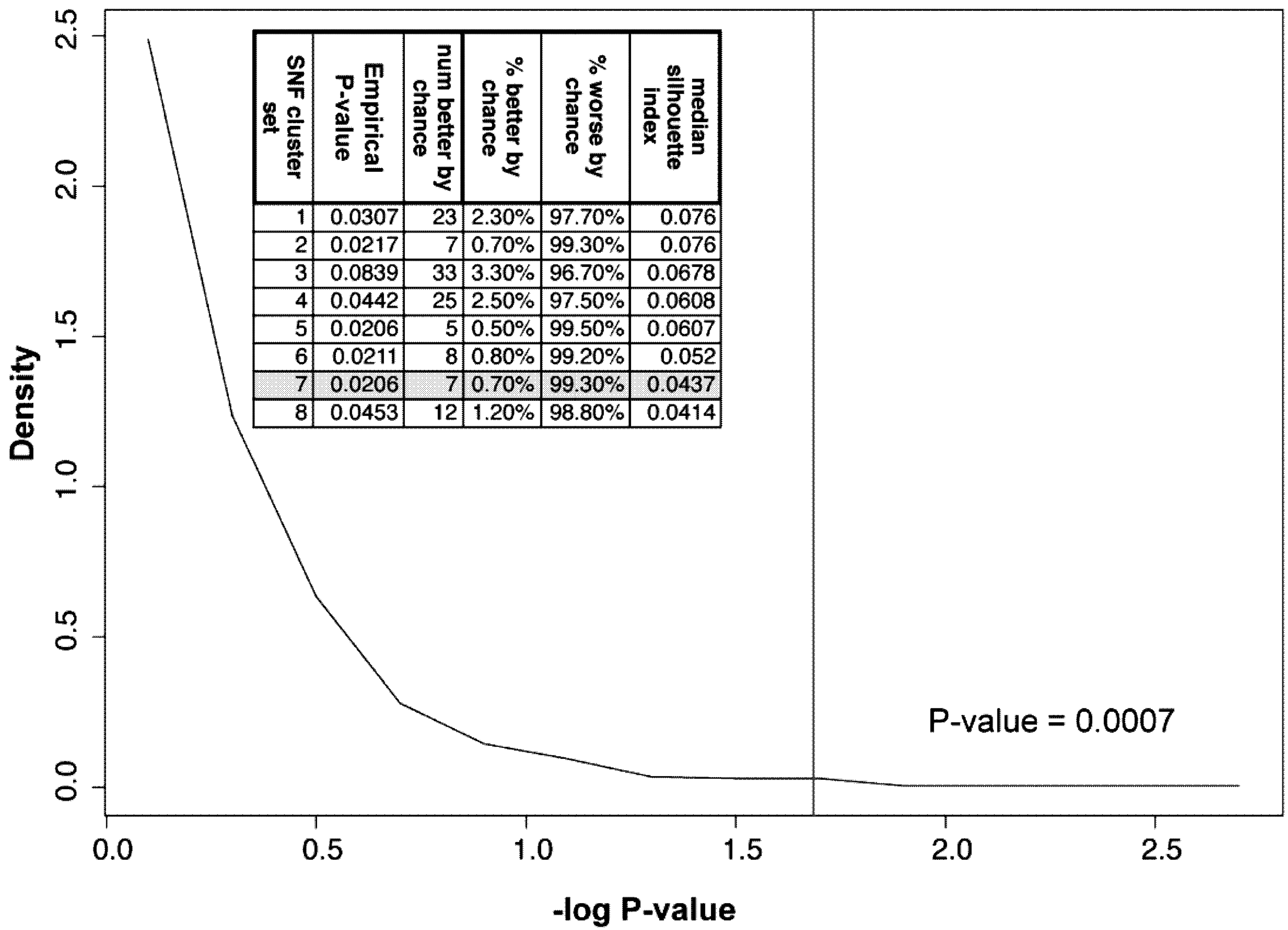
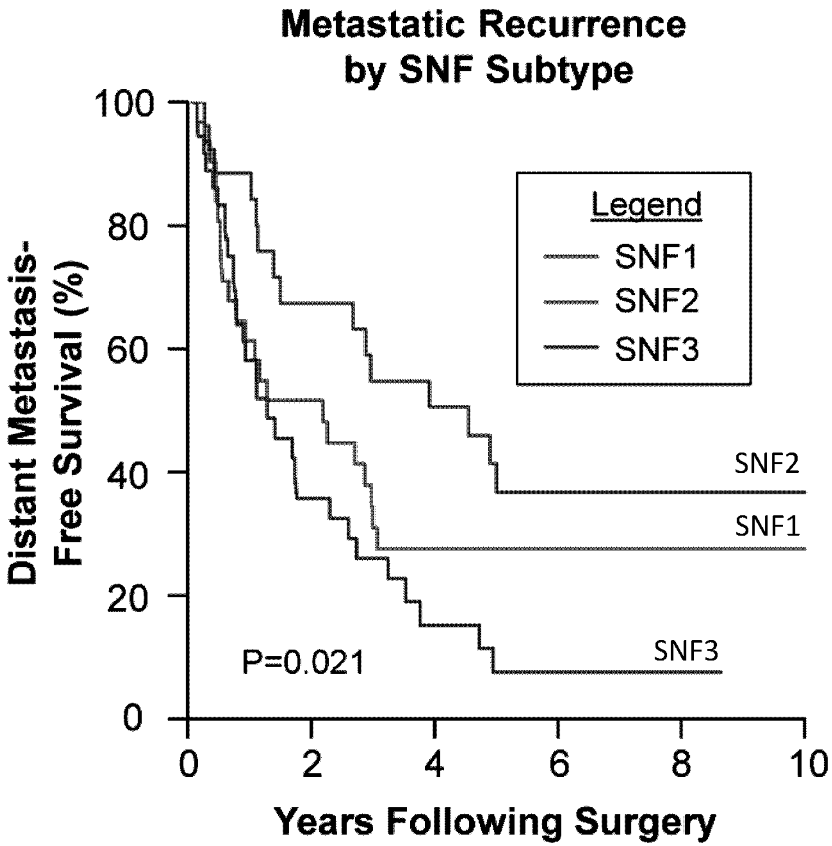

Primary CRC Anatomic Location
Frequency
100%
50%
0%
82
18
58
42
75
25
SNF1 SNF2 SNF3
Right-sided
Left-sided
Metastatic Presentation
Frequency
100%
50%
0%
52
48
69
31
56
44
SNF1 SNF2 SNF3
Synchron.
Metachron.
Largest Liver Met Size
Frequency
100%
50%
0%
65
35
73
27
*
86
14
SNF1 SNF2 SNF3
size>5cm
size<=5cm
Metastasis Histological Grade
Frequency
100%
50%
0%
15
85
5
95
27
73
SNF1 SNF2 SNF3
Grade1,2
Grade3
Recurrence Status
Frequency
100%
50%
0%
39
61
46
54
25
75
SNF1 SNF2 SNF3
Recurrent
Non-recurrent
Sites of Metastatic Recurrence
Frequency
100%
50%
0%
74
26
50
50
52
48
SNF1 SNF2 SNF3
Hepatic
Extrahepatic

FIG. 10B



SNF cluster set	Empirical P-value	num better by chance	% better by chance	% worse by chance	median silhouette index
1	0.0307	23	2.30%	97.70%	0.076
2	0.0217	7	0.70%	99.30%	0.076
3	0.0839	33	3.30%	96.70%	0.0678
4	0.0442	25	2.50%	97.50%	0.0608
5	0.0206	5	0.50%	99.50%	0.0607
6	0.0211	8	0.80%	99.20%	0.052
7	0.0206	7	0.70%	99.30%	0.0437
8	0.0453	12	1.20%	98.80%	0.0414

FIG. 11



No. at risk

SNF1	31	16	9	7	5	2
SNF2	26	17	13	9	9	5
SNF3	36	12	5	3	2	1

FIG. 12

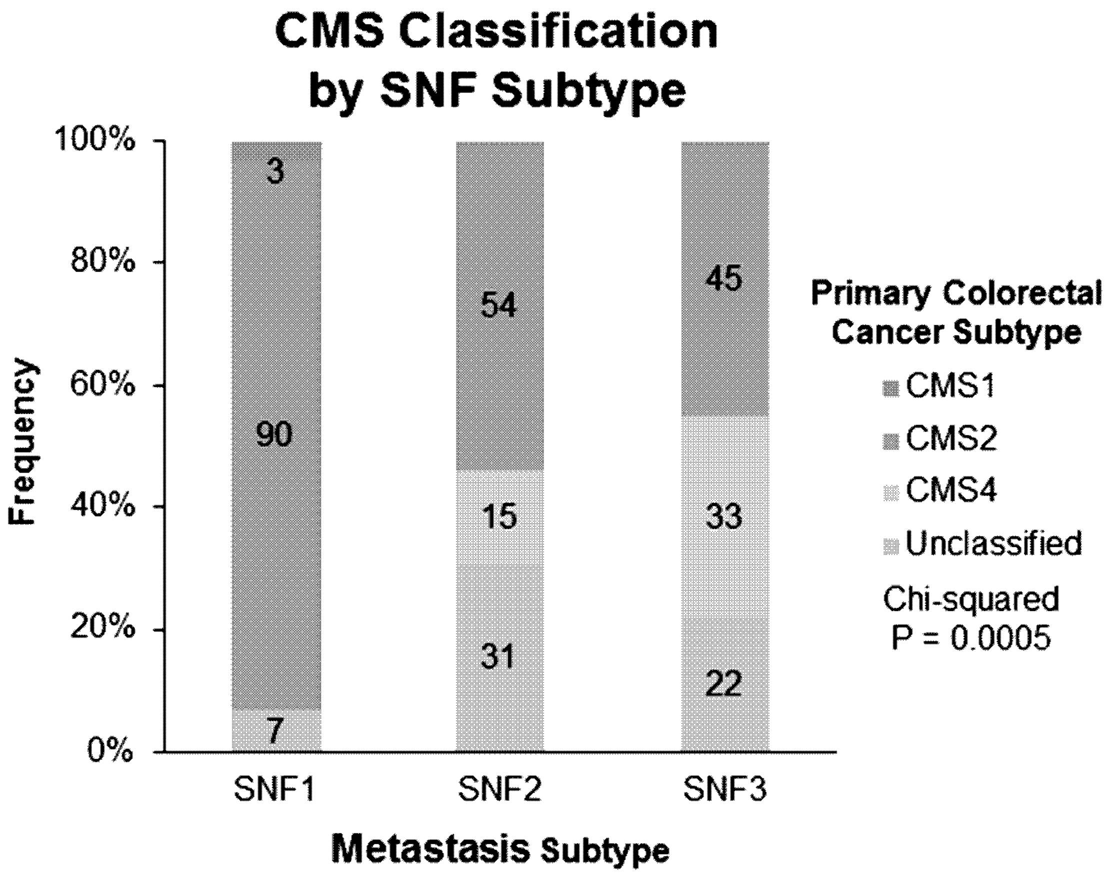

CMS Classification
by SNF Subtype
100%
80%
60%
40%
20%
0%
Frequency
3
90
7
54
15
31
45
33
22
SNF1
SNF2
SNF3
Metastasis Subtype
Primary Colorectal Cancer Subtype
CMS1
CMS2
CMS4
Unclassified
Chi-squared
P = 0.0005

FIG. 13

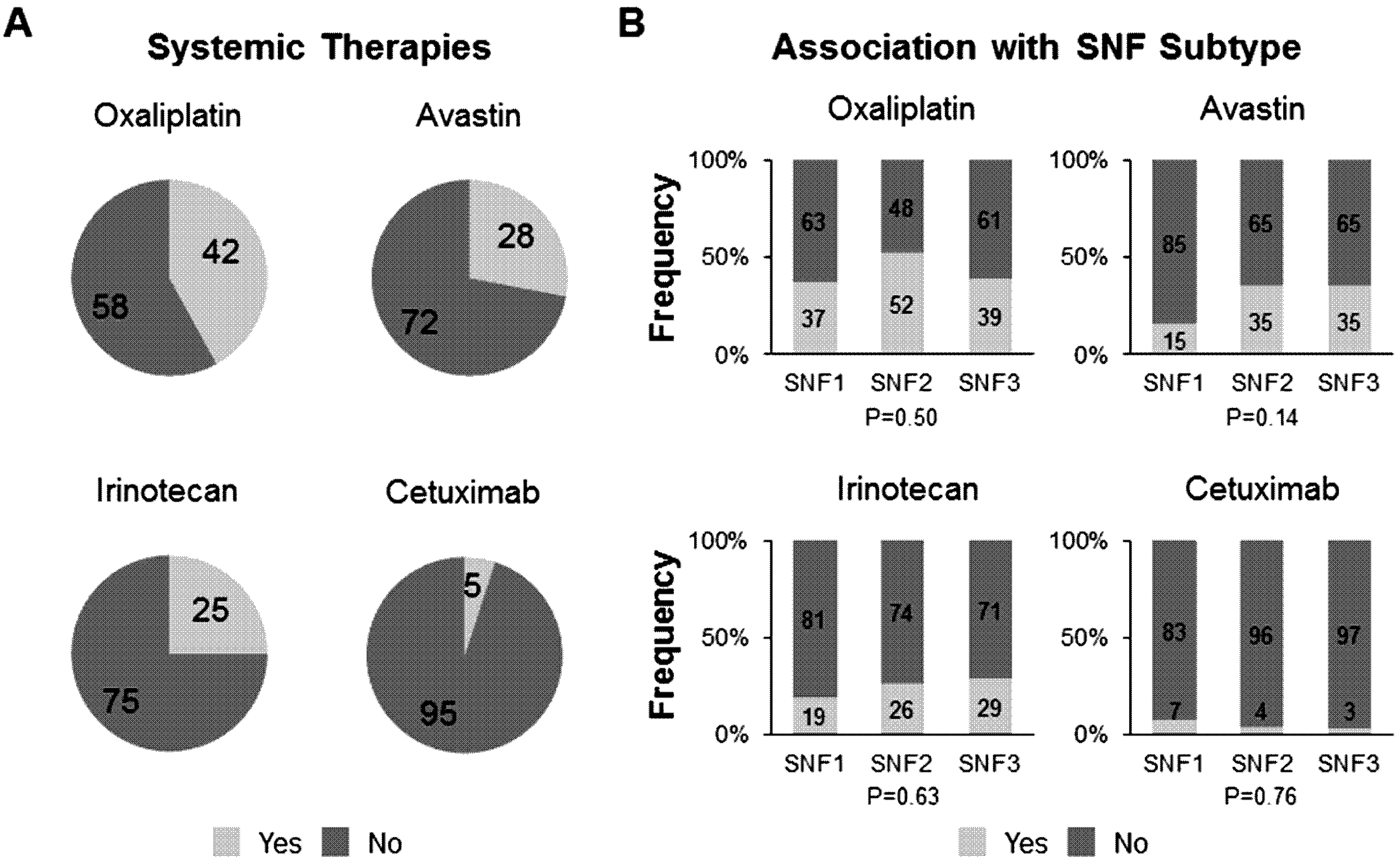

A
Systemic Therapies
Oxaliplatin
42
58
Avastin
28
72
Irinotecan
25
75
Cetuximab
5
95
Yes
No
B
Association with SNF Subtype
Oxaliplatin
Frequency
100%
50%
0%
63
37
48
52
61
39
SNF1
SNF2
SNF3
P=0.50
Avastin
100%
50%
0%
85
15
65
35
65
35
SNF1
SNF2
SNF3
P=0.14
Irinotecan
Frequency
100%
50%
0%
81
19
74
26
71
29
SNF1
SNF2
SNF3
P=0.63
Cetuximab
100%
50%
0%
83
7
96
4
97
3
SNF1
SNF2
SNF3
P=0.76
Yes
No

FIG. 14A-B

A

Performance metrics	Values
Accuracy	0.864(95% CI: 0.651, 0.971)
Balanced Accuracy	0.906
Sensitivity	1
Specificity	0.812
Positive Prediction Value (PPV)	0.667
Negative Prediction Value (NPV)	1
Cohen's Kappa	0.703
Matthew's Correlation Coefficient	0.736
AUC	0.875

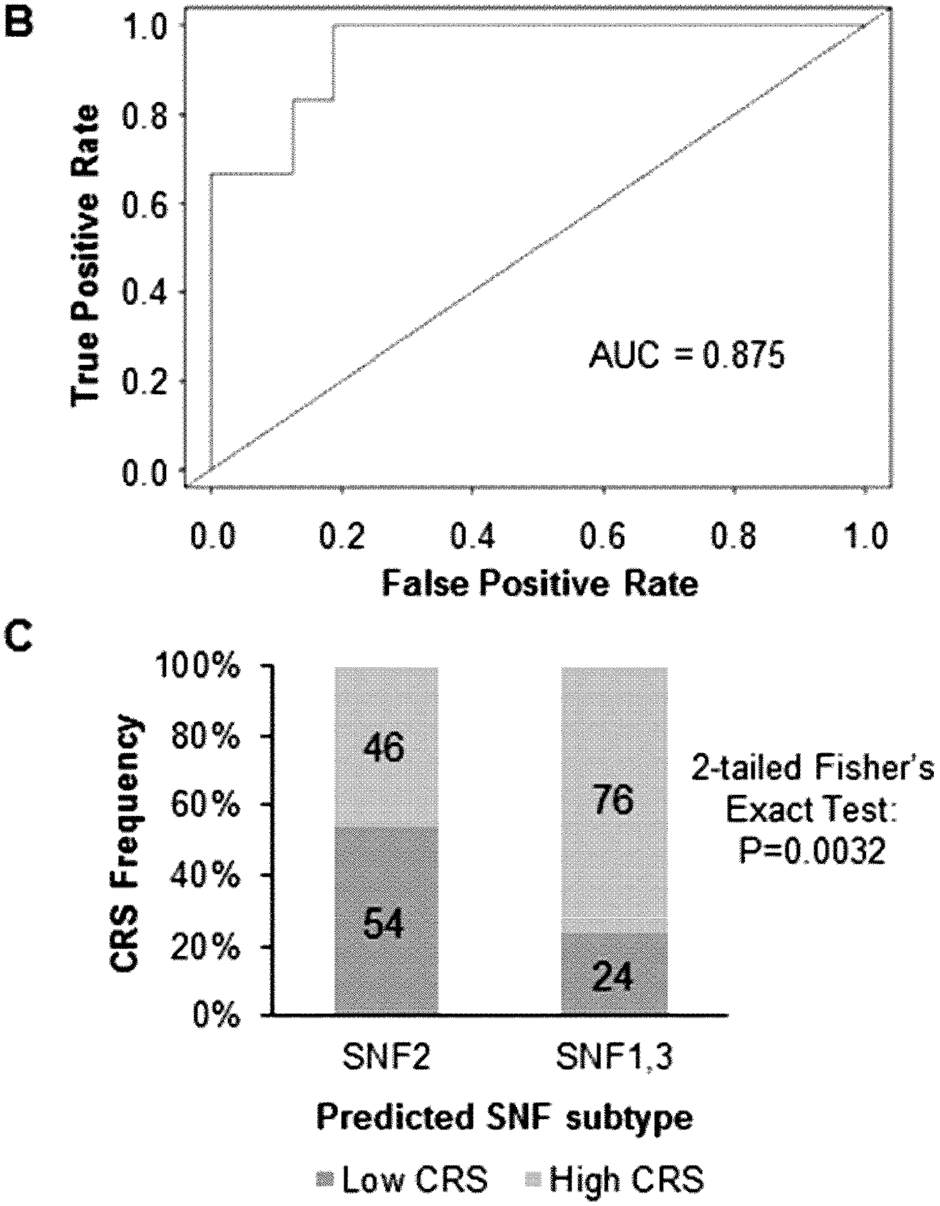


FIG. 15A-C

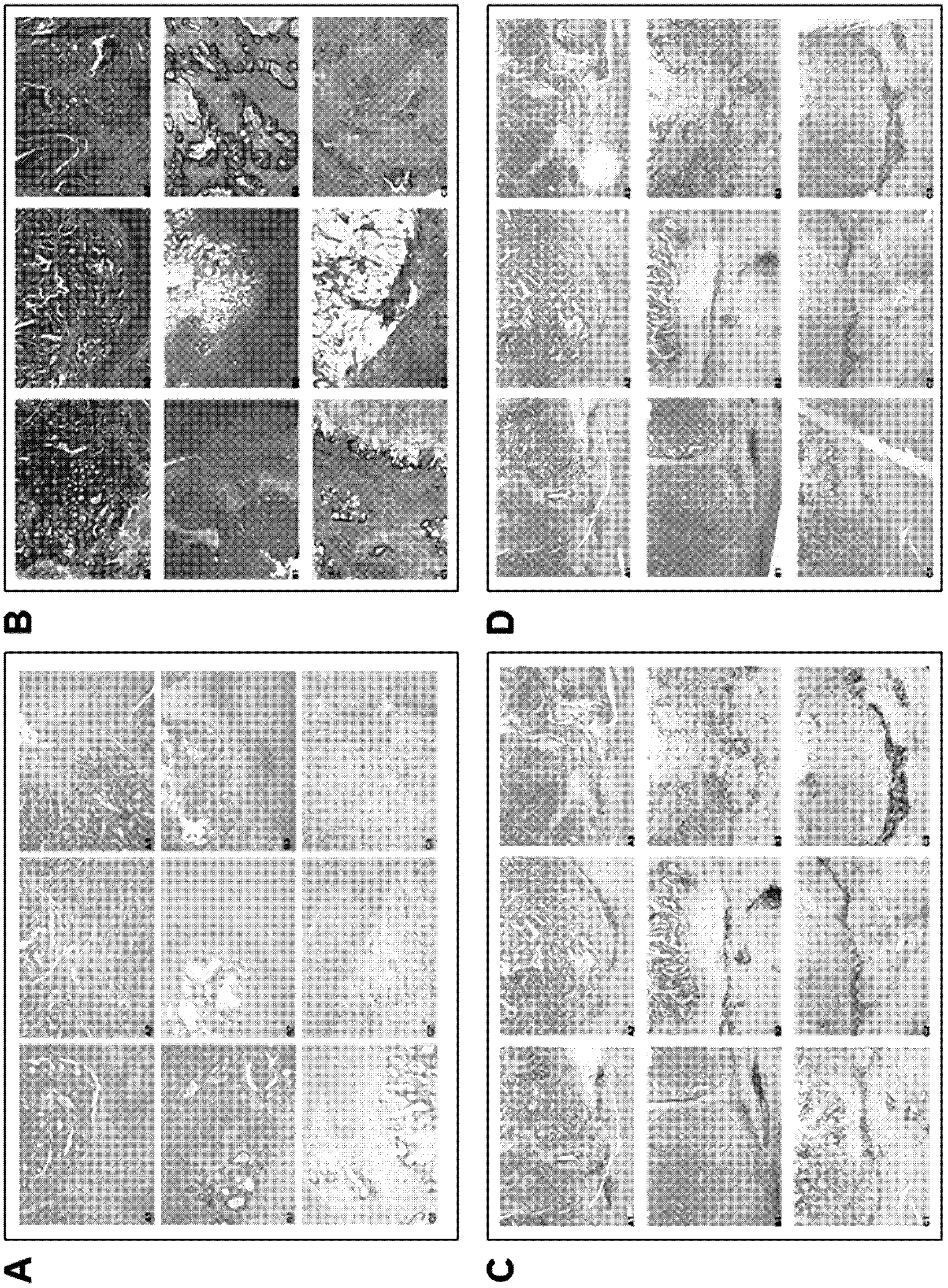


FIG. 16A-D

Mutational Patterns in Colorectal Liver Metastases

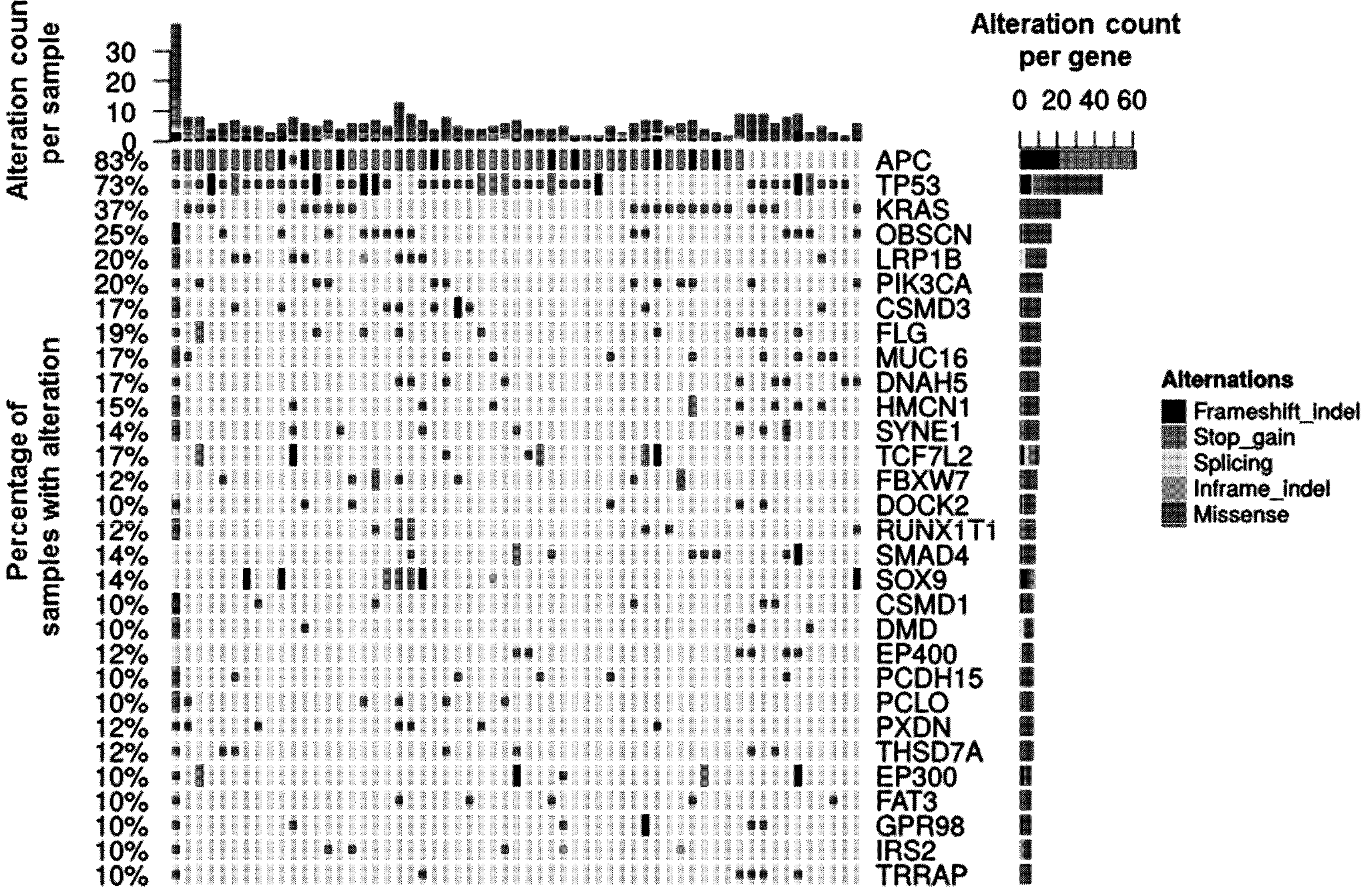


FIG. 17

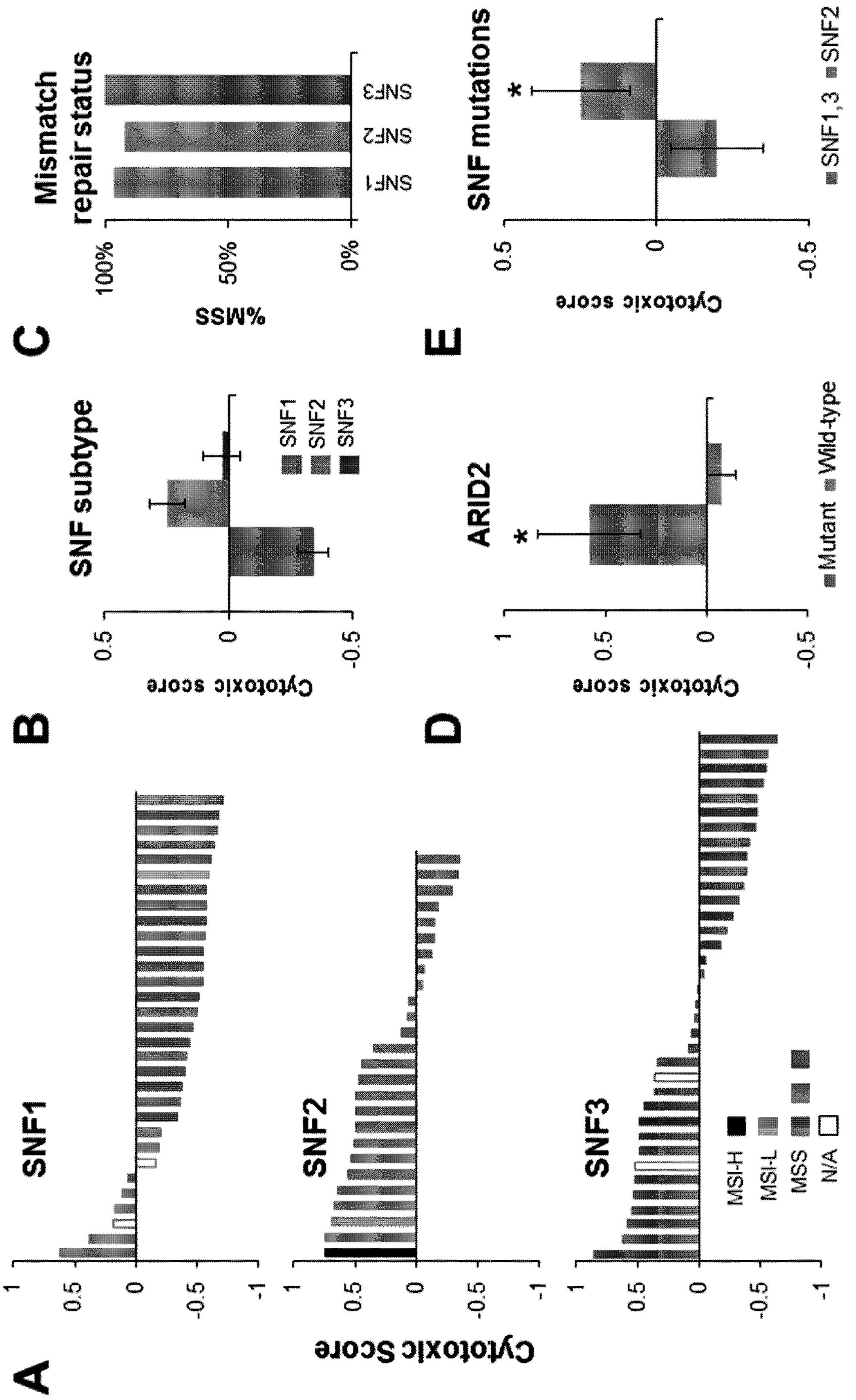
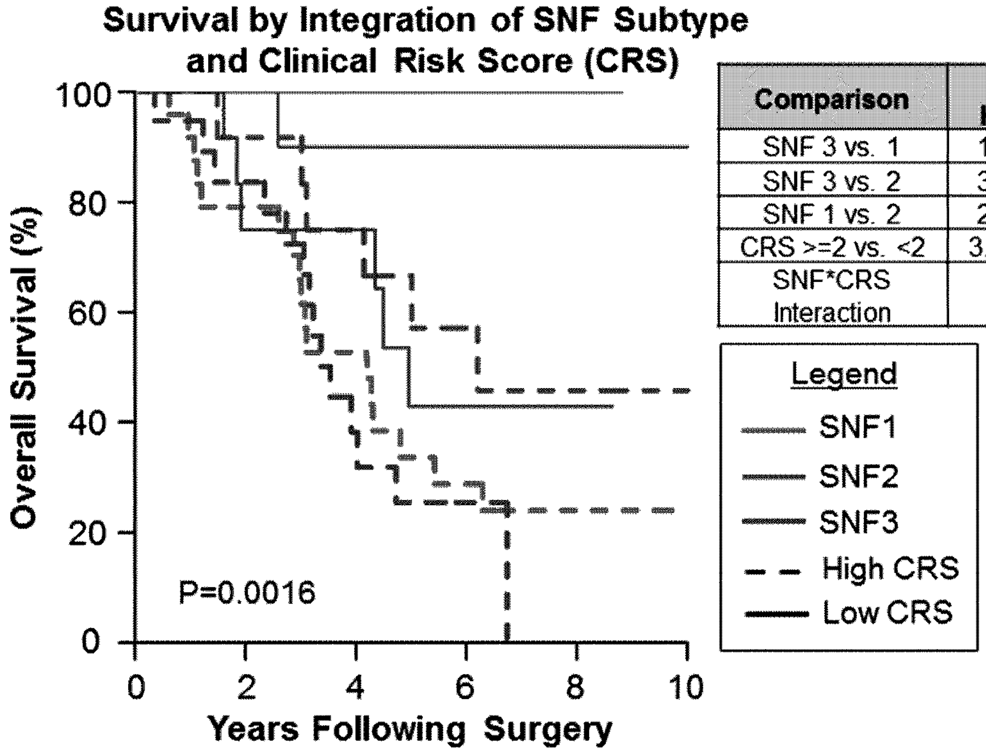

A
Cytotoxic Score
SNF1
SNF2
SNF3
1
0.5
0
-0.5
-1
MSI-H
MSI-L
MSS
N/A
B
SNF subtype
Cytotoxic score
0.5
0
-0.5
SNF1
SNF2
SNF3
C
Mismatch repair status
%MSS
100%
50%
0%
SNF1
SNF2
SNF3
D
ARID2
Cytotoxic score
1
0.5
0
-0.5
*
Mutant
Wild-type
E
SNF mutations
Cytotoxic score
0.5
0
-0.5
*
SNF1,3
SNF2

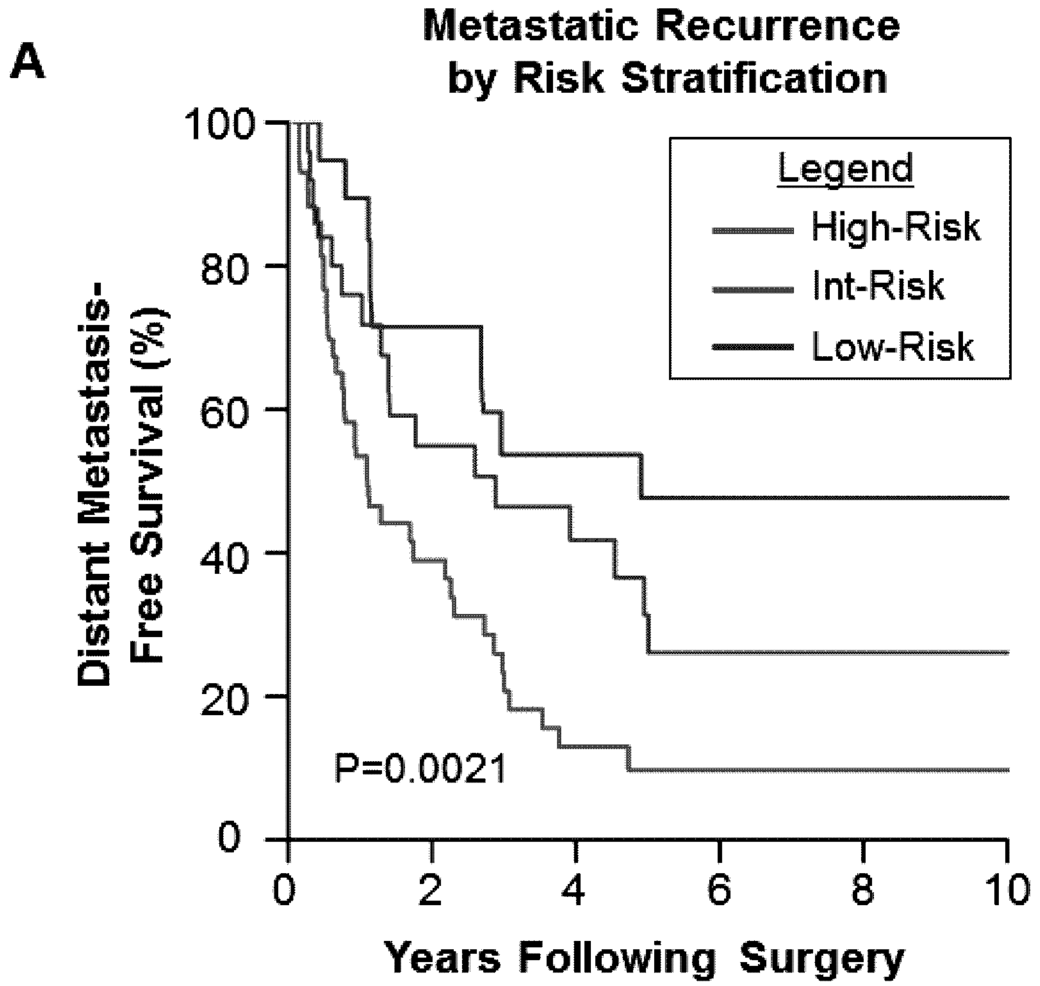
FIG. 18A-E



Comparison	Multivariate Hazard Ratio	P-value
SNF 3 vs. 1	1.54 (0.80-3.0)	0.1991
SNF 3 vs. 2	3.08 (1.35-7.9)	0.0068
SNF 1 vs. 2	2.00 (0.86-5.2)	0.1104
CRS >=2 vs. <2	3.66 (1.72-9.06)	0.0004
SNF*CRS Interaction	N/A	0.08

No. at risk							
SNF1-lowCRS	7	7	5	4	2	1	Low-Risk
SNF2-lowCRS	12	11	8	8	8	4	
SNF2-highCRS	12	12	10	6	5	3	Intermediate-Risk
SNF3-lowCRS	13	10	8	5	2	1	
SNF1-highCRS	24	19	13	7	5	3	High-Risk
SNF3-highCRS	19	16	7	2	1	1	

FIG. 19



No. at risk

Low-Risk	19	13	10	8	6	3
Int-Risk	25	14	10	6	5	2
High-Risk	43	16	6	4	4	2

FIG. 20A

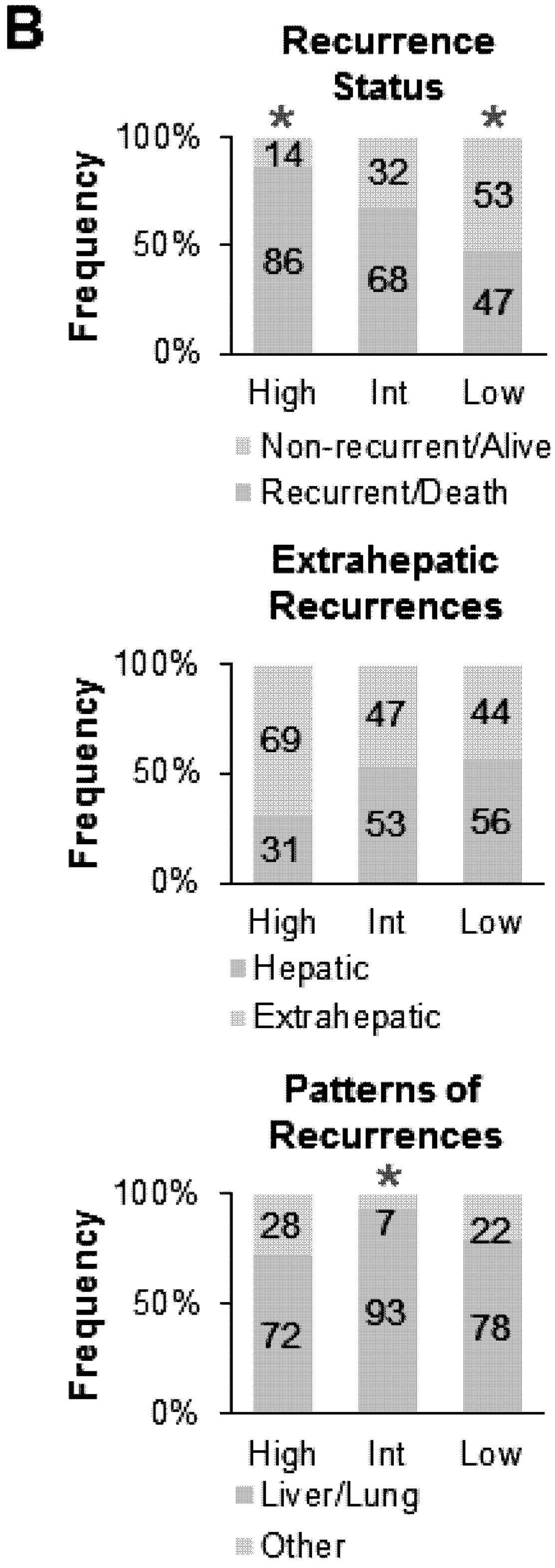

B
Recurrence Status
*
*
100%
50%
0%
Frequency
14
86
32
68
53
47
High
Int
Low
Non-recurrent/Alive
Recurrent/Death
Extrahepatic Recurrences
100%
50%
0%
Frequency
69
31
47
53
44
56
High
Int
Low
Hepatic
Extrahepatic
Patterns of Recurrences
*
100%
50%
0%
Frequency
28
72
7
93
22
78
High
Int
Low
Liver/Lung
Other

FIG. 20B

METHODS AND KITS FOR DIAGNOSIS AND TRIAGE OF PATIENTS WITH COLORECTAL LIVER METASTASES

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of priority of U.S. Provisional Patent Application No. 62/659,936 filed Apr. 19, 2018, which is hereby incorporated by reference in its entirety.

BACKGROUND OF THE INVENTION

1. Field of the Invention

[0002] The current disclosure relates generally to molecular biology and medicine. Particularly it concerns the field of oncology. More particularly, the disclosure relates to methods, compositions and kits involving diagnosis and treatment of metastatic cancer, including metastatic colorectal cancer.

2. Technical Background

[0003] Metastases are the leading cause of cancer-related deaths and are frequently widely disseminated, which has led to the prevailing view that metastases are always widespread. The oligometastasis hypothesis suggests that metastatic spread is a spectrum of virulence where some metastases are limited both in number and organ involvement and potentially curable with surgical resection or other locoregional therapies[1,2]. This paradigm is in stark contrast to the outcomes of patients with solid tumors where widespread metastases are largely fatal despite recent advances in systemic therapy. To date, the oligometastasis concept has been challenged, in large part, due to the lack of supporting molecular data to identify metastases associated with restricted spread[3,4].

[0004] Limited metastasis is relatively common. Data from clinical trials and single institution analyses of lung, breast, colorectal, prostate and renal cancers suggest that as many as 40-60% of patients with metastasis present with or develop limited disease[5-8]. Patients with limited liver metastases from colorectal cancer (CRC) have been consistently demonstrated to achieve prolonged survival after hepatic resection[9,10] and provide an opportunity to investigate the molecular basis for oligometastasis. While there have been extensive investigations into the molecular subtypes of primary human cancers, little is known regarding molecular subtypes of metastasis and their relation to clinical outcomes.

[0005] There is a need for the identification of a molecular basis for differing outcomes among metastatic cancer patients, for the ability to identify molecular subtypes of metastatic cancer that are predictive of the clinical outcome, and for the identification of integrated molecular patterns in liver metastases that are associated with long-term survival. There is also a need for methods to differentially identify patients with potentially curable oligometastatic disease from those whose few metastases are a part of a large cascade of widespread disease. The identification of these subtypes of metastatic disease can help in deciding on an appropriate treatment plan for a particular patient.

SUMMARY OF THE INVENTION

[0006] The inventors have discovered a molecular basis for oligometastasis that is predictive of clinical outcome and have developed methods of diagnosis, prognosis, and treatment that use the molecular classification of metastatic tissue to identify curable metastatic cancer and otherwise guide treatment decisions. Using integrated analysis of gene and miRNA expression data in metastatic tissue samples, the inventors identified three molecular subtypes of colorectal cancer metastases. The three subtypes correlate with different clinical outcomes, and knowing the subtype of the metastasis informs treatment decisions and helps provide an accurate assessment of patient prognosis. This discovery applies in metastatic cancers beyond only colorectal liver cancer—methods disclosed herein can be used to identify molecular subtypes of other metastatic cancers and to guide prognosis and treatment decisions for patients having such cancers.

[0007] Disclosed herein is a method comprising measuring expression levels of one or more genes listed in Table 10A or one or more miRNAs listed in Table 11A in a sample comprising tissue from a metastasis from a primary cancer tumor. These tables list genes and miRNAs whose expression is particularly valuable in classifying molecular subtypes of metastases. In some embodiments, expression of other genes and miRNAs are also measured. For example, any of the methods disclosed herein may involve measuring the expression of one or more genes listed in Tables 3A-C, which list genes that are differentially expressed in SNF1, SNF2, and SNF3 liver metastases from colorectal cancer primary tumors. Any of the methods disclosed herein may also include measuring expression of one or more miRNAs listed in Tables 4A-4C, which lists miRNAs that are differentially expressed in SNF1, SNF2, and SNF3 liver metastases from colorectal cancer primary tumors. Any of the methods disclosed herein may also include measuring expression of the genes listed in Table 7 (immune genes overexpressed in SNF2 metastases). In some embodiments, the methods disclosed herein also include determining whether one or more of the genes listed in Table 8 are mutated or whether one or more of the genomic alterations listed in Table 9 are present. In some embodiments, expression of both genes and miRNAs are measured as part of a method disclosed herein. The methods disclosed herein can be used specifically in the context of metastatic colorectal cancer. Thus, in some embodiments, the metastasis may be a liver metastasis, and the cancer may be colorectal cancer. The metastasis that is tested may also be in other parts of the body besides the liver, including the lung, peritoneum, brain, or bone. The methods disclosed herein can also be used in the context of other metastatic cancers including, for example, liver cancer, testicular cancer, biliary cancer, ovarian cancer, urinary tract cancer, pancreatic cancer, prostate cancer, esophageal cancer, gastric cancer, head and neck cancer, cervical cancer, lung cancer, neuroendocrine cancer, kidney cancer, breast cancer, and melanoma.

[0008] In some embodiments, the expression levels of at least, at most, or exactly 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 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, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, or 113 of the genes listed in Table 10A are measured, or any range derivable therein. In some embodiments, the expression levels of at least, at most, or exactly 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 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, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, or 113 of the genes listed in Table 10A are excluded from being measured, or any range derivable therein. In some embodiments, the expression levels of at least, at most, or exactly 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 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, or 53 of the miRNAs listed in Table 11A are measured, or any range derivable therein. In some embodiments, the expression levels of at least, at most, or exactly 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 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, or 53 of the miRNAs listed in Table 11A are excluded from being measured, or any range derivable therein.

[0009] It is contemplated that expression levels of any subset of the genes or miRNAs listed in Tables 3A-C, 4A-C, 10A, and 11A may be measured or may be excluded from being measured as part of a method disclosed herein. Certain subsets of these genes and miRNAs may be chosen for their greater usefulness in making classifications and differentiating between different types of metastases. A subset of genes or miRNAs that are to be examined as part of an assay to identify a sample metastasis as belonging to a particular molecular subtype may be identified by an analysis such as a nearest shrunken centroid analysis to identify subsets of genes and/or miRNAs, or a combination of genes and miRNAs, whose expression levels best characterize each subtype. Methods disclosed herein may include performing such an analysis to identify a set of genes and/or miRNAs that can provide for accurate and sensitive subtyping of individual metastases. In some embodiments, expression of a subset of at least, at most, or exactly 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 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, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 210, 220, 230, 240, 250, 260, 270, 280, 290, 300, 310, 320, 330, 340, 350, 360, 370, 380, 390, 400, 410, 420, 430, 440, 450, 460, 470, 480, 490, 500, 510, 520, 530, 540, 550, 560, 570, 580, 590, 600, 610, 620, 630, 640, 650, 660, 670, 680, 690, 700, 710, 720, 730, 740, 750, 760, 770, 780, 790, 800, 810, 820, 830, 840, 850, 860, 870, 880, 890, 900, 910, 920, 930, 940, 950, 960, 970, 980, 990, or 1000 genes or miRNAs listed in Tables 3A-C and 4A-C, or any range derivable therein, are examined.

[0010] In some embodiments, the expression levels of one or more genes or one or more miRNAs are within a predetermined amount of the mean expression levels of the one or more genes or miRNAs, on a gene-by-gene and miRNA-by-miRNA basis, in metastases of a cohort of patients having an oligometastatic phenotype, of a cohort of patients who are likely to be healed without the administration of systemic cancer therapy, or of a cohort of patients having a mean ten-year overall survival expectation that is at least 60%. The mean levels may be determined by measuring the expression levels of genes in metastases of patients in the cohort and calculating a mean expression level for each gene. In some embodiments, the patients are patients having metastatic cancer or having metastatic colorectal cancer. Classification of a metastasis may be done by comparing the measured expression levels of genes and/or miRNAs to reference expression levels of the same genes and/or miRNAs. The reference expression levels may be identified as the mean expression levels in metastases of a cohort of patients having characteristics associated with a metastatic subtype, such as a cohort having a mean ten-year overall survival expectation that is at least 60%, or other characteristics of a molecular subtype, such as the characteristics of an SNF1, SNF2, or SNF3 subtype described herein. The reference expression levels of such cohorts, and of any patient cohorts described herein, may be established by measuring the expression levels in metastases of at least, at most, or exactly 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 600, 700, 800, 900, or 1000 subjects in the cohort, or any range derivable therein. In some embodiments, the cohort of patients comprises a representative sample of metastatic cancer patients, including metastatic colorectal cancer patients, having a certain characteristic, such as an oligometastatic phenotype, a relatively high likelihood of being successfully treated with immune checkpoint therapy, a mean ten-year survival expectation of at least 60%, or other characteristics of metastatic subtypes identified herein. If the expression levels of the genes and/or miRNAs measured in a sample metastasis are sufficiently close to the reference expression levels of a metastatic subtype, then the sample metastasis can be classified as being of that subtype. The degree of closeness in expression levels required to be classified as a match may be predetermined using a statistical analysis. In some embodiments, the predetermined amount of closeness is within one standard deviation of the mean expression level of the reference cohort. In some embodiments, the predetermined amount is within 0.1, 0.5, 1.0, 2.0, 3.0, 4.0, 5.0, 10, 15, or 20% of the reference expression level, or any range derivable therein. In some embodiments, a sample metastasis may be classified as belonging to a molecular subtype despite the expression levels of one or more genes or miRNAs deviating from a reference expression level by a substantial amount. For instance, if a substantial number of other gene or miRNA expression levels sufficiently match the reference expression, then the sample metastasis may be classified as belonging to the subtype. A computer-based classifier programmed to perform a statistical analysis may be used to determine whether expression levels of a sufficient number of genes and/or miRNAs in a sample metastasis are sufficiently close to the reference expression levels of a particular molecular subtype to classify the sample as belonging to that subtype.

[0011] It is contemplated that the methods described herein may involve a comparison between expression levels measured for a sample metastasis and reference expression levels that are indicative of metastatic subtypes or any of the characteristics of metastatic subtypes described herein. Thus, in some embodiments, the measured expression level for a gene or miRNA is lower than, higher than, close to, higher by a predetermined amount than, lower by a predetermined amount than, or within a predetermined amount of the expression level of the gene or miRNA in metastases from a cohort of metastatic cancer patients having any one of the following characteristics: (i) a mean ten-year overall survival expectation of at least 60%; (ii) a relatively high or low likelihood of experiencing metastatic recurrence after hepatic resection; (iii) a relatively high or low likelihood of being successfully treated without systemic cancer treatments; (iv) a relatively low likelihood of being successfully treated with local cancer treatments; (v) a relatively high likelihood of being successfully treated with immune checkpoint therapy; (vi) a mean ten-year overall survival expectation of less than 50%, 35%, or 20%; (vii) a relatively high degree of infiltration of immune cells; among other characteristics of the metastatic subtypes described herein. In some embodiments, wherein the expression levels of one or more genes listed in Table 10A or one or more miRNAs listed in Table 11A deviate by a predetermined amount from the mean expression levels of the one or more genes or the one or more miRNAs in metastases of a cohort of metastatic colorectal cancer patients having a mean ten-year overall survival expectation that is less than 50%. In some embodiments, the expression levels of one or more genes listed in Table 10B are higher by a predetermined amount than the mean expression level of the one or more genes in metastases of a cohort of metastatic colorectal cancer patients having a mean ten-year overall survival expectation that is less than 50%. In some embodiments, the measured expression levels of one or more genes listed in Table 10C are lower by a predetermined amount than the mean expression level of the one or more genes in metastases of a cohort of metastatic colorectal cancer patients having a mean ten-year overall survival expectation that is less than 50%. In some embodiments, the measured expression levels of one or more miRNAs listed in Table 11B are higher by a predetermined amount than the mean expression level of the one more more miRNAs in metastases of a cohort of metastatic colorectal cancer patients having a mean ten-year overall survival expectation that is less than 50%. In some embodiments, the measured expression levels of one or more miRNAs listed in Table 11C is lower by a predetermined amount than the mean expression level of the one or more miRNAs in metastases of a cohort of metastatic colorectal cancer patients having a mean ten-year overall survival expectation that is less than 50%. In any of the methods described herein, a cohort of patients may be a cohort of metastatic cancer patients, colorectal cancer patients, or metastatic colorectal cancer patients.

[0012] In some embodiments, the method further comprises calculating a Clinical Risk Score ("CRS") for the patient, which is calculated using the following adverse clinical and pathological features: (1) disease-free interval between primary tumor diagnosis and development of metastasis <12 months, (2) number of liver metastases >1, (3) largest liver metastasis >5.0 cm, (4) lymph node-positive primary CRC, and (5) CEA>200 ng/mL. A patient with none of these features has a CRS of 0; a patient with one of these features has a CRS of 1; and so on up to a maximum CRS of 5.

[0013] In some embodiments, the method further comprises administering a cancer therapy to the patient. The cancer therapy may be chosen based on the gene or miRNA expression measurements, alone or in combination with the clinical risk score calculated for the patient. In some embodiments, the cancer therapy comprises a local cancer therapy. In some embodiments, the cancer therapy excludes a systemic cancer therapy. In some embodiments, the cancer therapy excludes a local therapy. In some embodiments, the cancer therapy comprises a local cancer therapy without the administration of a system cancer therapy. In some embodiments, the cancer therapy comprises an immunotherapy, which may be an immune checkpoint therapy. Any of these cancer therapies may also be excluded. Combinations of these therapies may also be administered. In some embodiments, the gene or miRNA expression measurement and analysis may indicate that one or more cancer therapies would be likely to be effective or ineffective. A particular advantage of methods disclosed herein is that they allow doctors for the first time to make a treatment decision based on the molecular subtype of a metastasis. The discoveries disclosed herein indicate that some metastatic subtypes, such as SNF2, for example, are more likely to respond to a local therapy such as resection, radiation therapy, and the like, without the need for a systemic cancer therapy, whereas it was previously thought that any metastatic cancer requires a systemic therapy. The discoveries disclosed herein also allow doctors to identify metastatic cancer for which a local therapy may not be helpful and/or for which systemic therapies, such as DNA damaging drugs, are appropriate.

[0014] Measuring the expression of genes and/or miRNAs may be done by a variety of methods. In some embodiments, the measurement comprises performing PCR using RNA obtained from a sample of metastatic tissue as a template. The method may include the use of sets of PCR primers that are complementary to sequences of genes or miRNAs listed in Tables 3A-C, 4A-C, 10A-C, or 11A-C, including any subsets thereof. Measuring expression may also comprise hybridizing nucleic acids to a microarray. The microarray may include nucleic acid sequences that correspond to or are complementary to sequences of genes or miRNAs listed in Tables 3A-C, 4A-C, 10A-C, or 11A-C, including any subsets thereof. Methods may also include the use of nucleic acid probes that correspond to or are complementary to sequences of genes or miRNAs listed in Tables 3A-C, 4A-C, 10A-C, or 11A-C. Any of the primers or probes used may be labeled or modified with fluorescent labels or other moieties that allow the primers or probes to be detected. In some embodiments, measuring expression comprises performing RNA sequencing.

[0015] Also disclosed is a method of treating metastatic cancer in a patient, the method comprising administering to the patient a local cancer therapy without administering systemic cancer therapy or administering to the patient an immunotherapy, wherein the patient has been determined to have expression levels of one or more genes listed in Table 10A or one or more miRNAs listed in Table 11B that are within a predetermined amount of the mean expression levels in metastases of a cohort of metastatic cancer patients having a mean overall ten-year survival expectation that is at least 60%. In some embodiments, the patient has been determined to have expression levels of at least, at most, or exactly 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, or 113 genes listed in Table 10A, or any range derivable therein, and/or at least, at most, or exactly 5, 10, 20, 30, 40, 50, or 53 miRNAs listed in Table 11A, or any range derivable therein, that are within a predetermined amount of the mean expression level in metastases of a cohort of metastatic cancer patients having a mean overall ten-year survival expectation that is at least 60%. In some embodiments, the treatments are administered to a patient that has been determined to have expression levels of one or more genes and/or miRNAs that are indicative of an oligometastatic phenotype or of other characteristics of SNF2 metastases. In some embodiments, the patient has been determined to have expression levels of at least, at most, or exactly 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, or 113 genes listed in Table 10A, or any range derivable therein, and/or at least, at most, or exactly 5, 10, 20, 30, 40, 50, or 53 miRNAs listed in Table 11A, or any range derivable therein, that are within a predetermined amount of the mean expression level of a cohort of metastatic cancer patients having a mean overall ten-year survival expectation that is at least 60%.

[0016] Also disclosed is a method of treating metastatic cancer in a patient, the method comprising administering to the patient a local cancer therapy without administering systemic cancer therapy, wherein the patient has been determined to have an mRNA and/or miRNA expression profile indicating an oligometastatic phenotype or a specific metastatic subtype that is likely to be successfully treated with local cancer therapy. In some embodiments, the mRNA expression profile is determined by determining the expression of one or more genes listed in Table 10A and the miRNA expression profile is determined by determining the expression of one or more genes listed in Table 11A. In some embodiments, the expression profile is determined by determining the expression levels of at least, at most, or exactly 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, or 113 genes listed in Table 10A, or any range derivable therein, and/or at least, at most, or exactly 5, 10, 20, 30, 40, 50, or 53 miRNAs listed in Table 11A, or any range derivable therein. In some embodiments, the expression profile indicates a ten-year survival expectation of greater than 60% or less than 50, 35, or 20%, an increased likelihood of successful treatment with administration of local cancer therapies, an increased infiltration of immune cells, or other characteristics of any metastatic subtype as described herein.

[0017] Also disclosed is a method of treating cancer in a patient having a metastasis from a primary cancer tumor, the method comprising: administering to the patient an immune checkpoint therapy or administering to the patient a local cancer therapy without administering a systemic cancer therapy, wherein the patient has been identified based on the expression levels of one or more mRNA and/or miRNA species in the metastasis as belonging to a group of patients with one or more of the following characteristics: (a) a mean ten-year overall survival expectation of at least 60%; (b) a likelihood of experiencing metastatic recurrence after hepatic resection that is lower than the likelihood for patients outside of the group; and (c) a level of immune cell infiltration into the metastasis that is higher than the mean level for patients outside the group. In some embodiments, the one or more mRNA species comprise one or more transcripts of the genes listed in Table 10A. In some embodiments, the one or more miRNA species comprise one or more transcripts of the miRNAs listed in Table 11A. In some embodiments, the mRNA or miRNA species comprise at least, at most, or exactly 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, or 113 genes listed in Table 10A, or any range derivable therein, and/or at least, at most, or exactly 5, 10, 20, 30, 40, 50, or 53 miRNAs listed in Table 11A, or any range derivable therein. In some embodiments, the metastasis is a liver metastasis and the cancer is colorectal cancer.

[0018] Also disclosed is a method of diagnosing a patient having a metastasis from a primary colorectal cancer tumor, the method comprising: (a) measuring the expression levels in the metastasis of one or more of the genes or of one or more miRNAs; (b) identifying the patient as having an oligometastatic phenotype, as being a responder to immune checkpoint cancer therapy, or as having a ten-year survival expectation of greater than 60% if the expression level of one or more of the genes or miRNAs is within a predetermined amount of a first reference expression level or deviates from a second reference expression level by a predetermined amount. In some embodiments, the first reference expression level represents the mean expression level in metastases of a cohort of metastatic cancer patients having an oligometastatic phenotype, being responders to immune checkpoint cancer therapy, and/or or having mean ten-year survival expectation of greater than 60%. In some embodiments, the second reference expression level represents the mean expression level in metastases of a cohort of metastatic cancer patients having a mean ten-year survival expectation of less than 50%. In some embodiments, the one or more genes and/or miRNAs comprise at least, at most, or exactly 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, or 113 genes listed in Table 10A, or any range derivable therein, and/or at least, at most, or exactly 5, 10, 20, 30, 40, 50, or 53 miRNAs listed in Table 11A, or any range derivable therein.

[0019] Also disclosed is a method of diagnosing and treating a patient having a metastasis from a primary colorectal cancer tumor, the method comprising: (a) obtaining a tissue sample from the metastasis; (b) measuring the expression of one or more genes and/or miRNAs in the sample; (c) comparing the measured expression level of each gene or miRNA to a reference expression level for that gene or miRNA; (d) identifying the metastasis as an SNF1, SNF2, or SNF3-type metastasis based on the measured expression levels; and (e) administering to the patient an appropriate therapy based on the type of metastasis identified in step (d). In some embodiments, the one or more genes and/or miRNAs comprise at least, at most, or exactly 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, or 113 genes listed in Table 10A, or any range derivable therein and/or at least, at most, or exactly 5, 10, 20, 30, 40, 50, or 53 miRNAs listed in Table 11A, or any range derivable therein. In some embodiments, the appropriate therapy for a patient with an SNF2-type metastasis comprises an immune checkpoint cancer therapy. In some embodiments, the appropriate therapy for a patient with an SNF2-type metastasis comprises a local cancer therapy unaccompanied by systemic cancer therapy. In some embodiments, the appropriate therapy for a patient with an SNF1 metastasis comprises a DNA-damaging cancer therapy. In some embodiments, the DNA-damaging cancer therapy comprises administering PARP inhibitors. In some embodiments, the appropriate therapy for a patient with an SNF1 or SNF3 metastasis comprises a systemic cancer therapy. In some embodiments, the appropriate therapy for a patient with an SNF1 or SNF3 metastasis excludes immune checkpoint cancer therapy.

[0020] Also disclosed is a method of providing a prognosis for a patient having metastatic colorectal cancer, the method comprising: (a) evaluating the expression of one or more genes and/or miRNAs in a tissue sample from a metastasis taken from the patient to identify the metastasis as an SNF1, SNF2, or SNF3-type metastasis; (b) determining the clinical risk score of the patient; (c) determining the ten-year survival expectation of the patient as follows: (i) identifying the patient as having a ten-year survival expectation of greater than 90% if the metastasis is type SNF1 or SNF2 and the clinical risk score is 0 or 1; (ii) identifying the patient as having a ten-year survival expectation of between 40 and 50% if the metastasis is type SNF2 and the clinical risk score is 2 or greater or if the metastasis is type SNF3 and the clinical risk score is 0 or 1; and (iii) identifying the patient as having a ten-year survival expectation of less than 24% if if the metastasis is type SNF1 or SNF3 and the clinical risk score is 2 or greater. In some embodiments, the genes and/or miRNAs comprise at least, at most, or exactly 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, or 113 genes listed in Table 10A, or any range derivable therein, and/or at least 5, 10, 20, 30, 40, 50, or 53 miRNAs listed in Table 11A, or any range derivable therein.

[0021] Also disclosed is a method comprising evaluating the expression levels of multiple mRNA and/or miRNA species in a sample comprising tissue from a liver metastasis of a patient that has metastatic colorectal cancer to identify the patient as belonging to a first group of metastatic colorectal cancer patients or a second group of metastatic colorectal cancer patients, wherein: (a) the first group has one or more of the following characteristics: (i) a mean ten-year overall survival expectation of at least 60%; (ii) a mean ten-year overall survival expectation that is higher than that for patients outside of the first group; (iii) a likelihood of experiencing metastatic recurrence after hepatic resection that is lower than the likelihood for patients outside of the first group; (iv) a likelihood of being successfully treated without systemic cancer treatments that is higher than the likelihood for patients outside of the first group; and (v) a likelihood of being successfully treated with immune checkpoint therapy that is higher than the likelihood for patients outside of the first group; and (b) the second group has one or more of the following characteristics: (i) a mean ten-year overall survival expectation of less than 50%; (ii) a mean ten-year overall survival expectation that is lower than that for patients outside of the second group; (iii) a likelihood of experiencing metastatic recurrence after hepatic resection that is higher than for patients outside of the second group; (iv) a likelihood of being successfully treated without systemic cancer treatments that is lower than the likelihood for patients outside of the second group; (v) a likelihood of being successfully treated with immune checkpoint therapy that is lower than the likelihood for patients outside of the second group; and (vi) a likelihood of being successfully treated with DNA damaging cancer therapy that is higher than the likelihood for patients outside of the second group. In some embodiments, the mRNA species comprise transcripts of one or more genes listed in Table 10A. In some embodiments, the miRNA species comprise one or more of the miRNAs listed in Table 11A. In some embodiments, the patient is identified as belonging to the first group of patients if the expression of one or more genes listed in Table 10A is within a predetermined amount of a reference expression level of the one or more genes. In some embodiments, the patient is identified as belonging to the first group of patients if the expression of one or more miRNAs listed in Table 11A is within a predetermined amount of a reference expression level of the one or more miRNAs. In some embodiments, step (b) comprises using a classifier that has been trained to identify an RNA expression pattern associated with the first group of patients. In some embodiments, the classifier evaluates the expression levels of at least, at most, or exactly 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, or 113 genes listed in Table 10A, or any range derivable therein. In some embodiments, the classifier evaluates the expression levels of at least, at most, or exactly 5, 10, 20, 30, 40, 50, or 53 of the miRNAs listed in Table 11A, or any range derivable therein. In some embodiments, the method further comprises administering an immune checkpoint therapy to a patient identified as belonging to the first group. In some embodiments, the method further comprises treating a patient identified as belonging to the first group with local treatment of liver metastases unaccompanied by systemic cancer treatment. In some embodiments, the method further comprises administering a DNA damaging cancer therapy to a patient identified as belonging to the second group of patients.

[0022] Also disclosed is a method of identifying a molecular subtype of metastatic cancer, the method comprising performing genome-wide expression profiling of a plurality of metastatic tissue samples to generate expression data of mRNA and miRNA in the tissue samples and analyzing the expression data using a similarity network fusion algorithm or other integrated molecular analysis technique that identifies similarities in both mRNA and miRNA expression data among samples to identify groups of samples having expression patterns that are similar to other samples in the group and that are dissimilar from samples outside the group. In some embodiments, the method further comprises identifying genes and miRNAs that are differentially expressed in a group of samples relative to either a mean expression level across all samples or a mean expression level of samples outside the group. In some embodiments, the method further comprises identifying a subset of the differentially expressed genes and/or miRNAs whose expression levels in a single sample can be used to accurately classify the sample as belonging to a particular molecular subtype or not belonging to a particular molecular subtype.

[0023] In any of the embodiments described herein, the patient may have already been diagnosed with cancer or already had tumor resection before any of the steps of methods described herein are performed.

[0024] Any step or aspect of an embodiment described herein may be implemented in the context of any other embodiment described herein

[0025] Other objects, features and advantages of the present invention will become apparent from the following detailed description. It should be understood, however, that the detailed description and the specific examples, while indicating specific embodiments of the invention, are given by way of illustration only, since various changes and modifications within the spirit and scope of the invention will become apparent to those skilled in the art from this detailed description.

BRIEF DESCRIPTION OF THE DRAWINGS

[0026] FIGS. **1**A-B show clinical outcomes following surgical resecton of limited liver metastases from colorectal cancer. Kaplan-Meier curves of overall survival by (A) clinical recurrence status (as determined by post-operative surveillance CT imaging and serum CEA measurements) or (B) Clinical Risk Scores (CRS) following hepatic resection of limited de novo CRCLM. Low CRS was defined as values less than two. P-values were determined using log-rank tests.

[0027] FIGS. **2**A-E show the identification of intrinsic molecular subtypes of colorectal liver metastases. (A) Consensus Molecular Subtypes (CMS) of primary colorectal cancers obtained from the Colorectal Cancer Subtyping Consortium (CRCSC) or calculated in primary colorectal cancers of The Cancer Genome Atlas (TCGA). CMS subtypes were also determined in colorectal liver metastases from patients undergoing partial hepatectomy of resectable liver metastases (UC, NS, MSK1 and MSK2 cohorts) or biopsy of unresectable liver metastases (MSK3, Italian and French cohorts). Cohorts contain independent clinical and molecular datasets. (B) Consensus clustering based on Similarity Network Fusion (SNF) subtyping of colorectal liver metastases. (C) Kaplan-Meier curves of overall survival by SNF subtype. P-value was determined using a log-rank test. (D) Metastatic recurrence patterns by SNF subtype. Asterisks denote statistical significance based on Fisher's exact test for each SNF subtype versus the two other SNF subtypes. (E) Differentially expressed mRNAs (left) and miRNAs (right) between the three SNF subtypes (see Tables 3A-C and 4A-C)

[0028] FIGS. **3**A-D show the molecular signatures of intrinsic subtypes of colorectal liver metastases. (A) Ensemble of Gene Set Enrichment Analyses (EGSEA) of significantly enriched 'Hallmark' and 'Cellular Estimate' gene signatures within each SNF subtype. Color intensity in EGSEA heatmaps is proportional to significance level (see Tables 5A-C and 6). SNF1=red, SNF2=green, SNF3=blue. (B) Functional categorization of differentially expressed immune genes overexpressed in SNF2. The SNF2 column indicates that many immune genes are overexpressed in SNF2, and the SNF1 and SNF3 columns indicate that many immune genes are suppressed in these subtypes. (C) OncoPrint plot of recurrent colorectal cancer mutations and copy number alterations by SNF subtype. (D) Frequencies of SNF-specific genomic alterations. Asterisks denote statistical significance based on Fisher's exact test comparing each SNF group to the two other SNF groups.

[0029] FIGS. **4**A-C show the integration of intrinsic molecular subtypes and clinical risk stratification. (A) Kaplan-Meier curves of overall survival following initial hepatic resection of limited de novo CRCLM based on integrated risk classification of SNF subtype and Clinical Risk Scores (CRS). P-value was determined using a log-rank test. (B) Metastatic recurrence patterns for integrated risk groups. Asterisks denote statistical significance based on Fisher's exact test for each individual group versus the two additional groups. (C) Proposed classification of colorectal liver metastasis based on SNF subtypes

[0030] FIG. **5**. Overview of study design.

[0031] FIG. **6**. Overall survival by Consensus Molecular Subtypes (CMS) in patients with colorectal liver metastases. CMS subtypes were determined for 93 patients in our cohort from RNA Sequencing data using the methodology implemented in Sage-Bionetwork's CMS classifier R package (see Example 7 for materials and methods). Kaplan-Meier survival analysis of 10-year overall survival was performed for patients with CMS2, CMS4 and unclassified patterns. One patient with a CMS1 pattern was excluded from survival analysis. No. at risk denotes the number of patients at risk at each specified time point. P-value was determined using a log-rank test across groups.

[0032] FIGS. **7**A-D. Consensus clustering analysis of the mRNA expression data for 95 patients with colorectal liver metastases. (A) Heatmaps of the consensus matrices for the predefined cluster numbers k (k=2, 3, 3, 4, 5, and 6); (B) Kaplan-Meier plot for 10-year overall survival of the patients stratified by their consensus cluster memberships. P-value was determined using a log-rank test across groups; (C) Consensus Cumulative Distribution Function (CDF) plot of the consensus matrix for each k, estimated by a histogram of 100 bins. The lower left portion of the CDF plot represents samples rarely clustered together, and the upper right portion represents those almost always clustered together, whereas the middle portion represents those with occasional co-assignments in different clustering runs; A flat middle segment, suggesting that very few sample pairs are ambiguous when k is correctly inferred, can be used to determine the optimal k of consensus clusters. (D) Proportion of ambiguous clustering (PAC) plot defined as the fraction of sample pairs with consensus index values falling in the intermediate sub-interval (0.1, 0.9). A low value of PAC indicates a flat middle segment in the CDF plot and is allowed to infer the optimal k (k=2).

[0033] FIGS. **8**A-D. Consensus clustering analysis of the miRNA expression data for 116 patients with colorectal liver metastases. (A) Heatmaps of the consensus matrices for the predefined cluster numbers k (k=2, 3, 3, 4, 5, and 6); (B) Kaplan-Meier plot for 10-year overall survival of the patients stratified by their consensus cluster memberships. P-value was determined using a log-rank test across groups; (C) Consensus Cumulative Distribution Function (CDF) plot of the consensus matrix for each k, estimated by a histogram of 100 bins. The lower left portion of the CDF plot represents samples rarely clustered together, and the upper right portion represents those almost always clustered together, whereas the middle portion represents those with occasional co-assignments in different clustering runs; A flat middle segment suggesting that very few sample pairs are ambiguous when k is correctly inferred, can be used to determine the optimal k of consensus clusters. (D) Proportion of ambiguous clustering (PAC) plot defined as the fraction of sample pairs with consensus index values falling in the intermediate sub-interval (0.1, 0.9). A low value of PAC indicates a flat middle segment in the CDF plot and is allowed to infer the optimal k (k=2).

[0034] FIG. **9**. Median Silhouette Index (SI) for the SNF clusters under 72 parameter settings. SI represents the separation distance between the resulting clusters under each parameter setting. The top 8 parameter settings with highest median SI (in red) were selected for further analysis, and the corresponding clustering results were used to determine the final SNF cluster memberships through majority voting.

[0035] FIGS. **10**A-B. Associations of SNF subtypes and clinicopathological variables. Statistical significance was assessed using Fisher's exact tests for categorical variables and Student's t-test for continuous variables. Asterisks denote P-values ≤0.05 in the comparison of one SNF subtype versus the remaining subtypes.

[0036] FIG. **11**. Non-random association of SNF network structure with overall survival in metastatic colorectal cancer patients. Shown is the density of the -log P-value for each simulation of the SNF cluster set with members closest to the consensus for illustrative purposes. The red line in the figure represents the empirical P-value for a particular parameter set (parameter settings: K=25, alpha=0.6, T=20). The table inset contains the key statistics for each of the top 8 SNF cluster parameterizations in order of decreasing median Silhouette Index; highlighted is a parameter setting which produced SNF clusters with memberships closest to the consensus SNF grouping differing only by two sample assignments.

[0037] FIG. **12**. Distant metastasis-free survival by SNF subtype. SNF subtypes were determined for 93 patients in our cohort. Kaplan-Meier survival analysis of distant metastasis-free survival (event=first metastatic recurrence or death). No. at risk denotes number of patients at risk at each specified time point. P-value was determined using a log-rank test across groups.

[0038] FIG. **13**. Primary CRC CMS subtype by SNF subtype. Shown is the distribution of primary colorectal cancer Consensus Molecular Subtypes (CMS) by SNF subtypes of colorectal liver metastases. CMS subtypes were determined for 93 patients in our cohort from RNA Sequencing data using the methodology implemented in Sage-Bionetwork's CMS classifier R package (see Example 7 for Methods and Materials). P-value denotes a Chi-Squared test across the three SNF groups.

[0039] FIGS. **14**A-B. Perioperative chemotherapy regimens and associations with SNF subtype. (A) Types of perioperative chemotherapies received by patients which were included in the integrated SNF analysis. Specific details regarding chemotherapy regimens were available for 81 of 93 patients. (B) Association between type of chemotherapy received in perioperative setting and molecular subtype of metastasis derived from SNF analysis. P-value denotes a Chi-Squared test across the three SNF groups.

[0040] FIGS. **15**A-C. Prediction Analysis of Microarrays (PAM)-based classifier to distinguish SNF subtypes. (A) Model evaluation on the test data set from our cohort samples. (B) The area under the ROC curve demonstrates the classification performance compared to a random classifier on the test data set (AUC=0.875 vs. AUC=0.50 for random classifier). (C) Mosaic plot showing the concordance between the predicted SNF cluster labels and the Clinical Risk Scores (CRS) in an independent data set of patients who underwent hepatic resection of limited colorectal liver metastases (Memorial Sloan-Kettering Cancer Center, n=96, ArrayExpress Identifier: E-MTAB-1951).

[0041] FIGS. **16**A-D. Histologic analysis by SNF subtypes of liver metastasis. (A) Hematoxylin and eosin, (B) Trichome, (C) CD3, and (D) CD8 staining by SNF subtype. Shown are 10× magnification fields for three representative patients from each SNF subtype. Top row, SNF1. Middle row, SNF2. Bottom row, SNF3.

[0042] FIG. **17**. Oncoprint plot of exomic mutations occurring in 59 patients with colorectal liver metastases. Genes mutated in ≥10% of samples are shown. Values to the left of the Oncoprint plot represent the percentage of samples that harbor a mutation (non-synonymous SNVs or indels) in a given gene. The horizontal bar plot indicates the number of mutations for each patient sample falling within these recurrently altered genes. The vertical bar plot to the right depicts the number of mutations seen in each gene across all 59 samples. 'Splicing' refers to mutations that affect a splice donor or acceptor site.

[0043] FIGS. **18**A-E. Cytotoxic immune signature by SNF subtypes. (A) Distribution of cytotoxic immune gene scores' by SNF subtype. MSI-H and MSI-L, microsatellite instability-high and -low. MSS, microsatellite stable. N/A, missing data. (B) Mean (±S.E.M.) values of cytotoxic cell immune scores by SNF subtype. (C) Percentage of MSS patients within each SNF subtype. Differences in cytotoxic immune scores by somatic ARID2 (D) or SNF-specific mutations (E). Metastases classified as harboring SNF2-specific mutations included CDK12, NRAS, and EBF1 mutations, whereas SMAD3, NOTCH1, or PIK3C2B mutations characterized SNF1, 3-specific mutations. Data represent mean±S.E.M. values. Asterisks denote P-values ≤0.05.

[0044] FIG. **19**. Overall survival by integration of SNF subtype and Clinical Risk Scores (CRS). High CRS denotes scores ≥2. Patient subgroups defined by SNF and CRS were classified into low-, intermediate-, and high-risk cohorts based on Kaplan-Meier analysis of overall survival rates. P-value was determined using a log-rank test across groups. No. at risk denotes number of patients at risk at each specified time point. Table inset denotes hazard ratios (95% confidence intervals) for Cox multivariate proportional hazard analysis of SNF and CRS (both as nominal variables). A multivariate interaction was assessed between SNF and CRS and removed from the final multivariate model due to non-significance. P-value was determined using likelihood ratio test.

[0045] FIGS. **20**A-B. Metastatic recurrence patterns by integrated risk classification. Risk groups were determined for 87 patients in our cohort. (A) Kaplan-Meier survival analysis of distant metastasis-free survival (event=first metastatic recurrence or death). P-value was determined using a log-rank test across groups. No. at risk denotes number of patients at risk at each specified time point. (B) Association of molecular/clinical risk stratification groups with patterns of metastatic recurrence. Statistical significance was assessed using Fisher's exact tests between one risk group versus the two remaining groups. Asterisks denote P-values ≤0.05.

DETAILED DESCRIPTION

[0046] Here, utilizing independent clinical cohorts of CRC patients who underwent resection of liver metastases, the inventors have identified integrated molecular patterns in liver metastases associated with long-term survival. The inventors' findings indicate a molecular basis for oligometastasis that is predictive of clinical outcome and complementary to established clinical risk factors associated with long-term survival following hepatic resection. Aspects of the current invention have important clinical implications in the selection of local therapy for those patients with potentially curable oligometastatic disease from those whose few metastases are a part of a large cascade of widespread disease. These concepts may be applicable to many histological types of cancer. Methods disclosed herein involve determining expression levels of genes and miRNAs in liver metastases to identify the molecular subtype of the metastasis. The subtype classification can be used to provide a prognosis and to guide treatment decisions. These and other aspects of the disclosed methods will be described in greater detail below.

A. GENE AND MIRNA EXPRESSION LEVELS

[0047] Methods disclosed herein include measuring expression of genes and/or miRNAs. Measurement of expression can be done by a number of processes known in the art. The process of measuring expression may begin by extracting RNA from a metastasis tissue sample. Extracted mRNA and/or miRNA can be detected by hybridization (for example by means of Northern blot analysis or DNA or RNA arrays (microarrays) after converting mRNA into labeled cDNA) and/or amplification by means of a enzymatic chain reaction. Quantitative or semi-quantitative enzymatic amplification methods such as polymerase chain reaction (PCR) or quantitative real-time RT-PCR or semi-quantitative RT-PCR techniques can be used. Primer pairs may be designed for the purpose of superimposing an intron to distinguish cDNA amplification from the contamination from genomic DNA (gDNA). Additional primers or probes, which are preferably labeled, for example with fluorescence, which hybridize specifically in regions located between two exons, are optionally designed for the purpose of distinguishing cDNA amplification from the contamination from gDNA. If desired, said primers can be designed such that approximately the nucleotides comprised from the 5' end to half the total length of the primer hybridize with one of the exons of interest, and approximately the nucleotides comprised from the 3' end to half the total length of said primer hybridize with the other exon of interest. Suitable primers can be readily designed by a person skilled in the art. Other amplification methods include ligase chain reaction (LCR), transcription-mediated amplification (TMA), strand displacement amplification (SDA) and nucleic acid sequence based amplification (NASBA). Expression levels of mRNAs and/or miRNAs may also be measured by RNA sequencing methods known in the art.

[0048] To normalize the expression values of one gene among different samples, comparing the mRNA level of the gene of interest in the samples from the subject object of study with a control RNA level is possible. As it is used herein, a "control RNA" is an RNA of a gene for which the expression level does not differ among different metastatic subtypes, for example a gene that is constitutively expressed in all types of cells. A control RNA is preferably an mRNA derived from a housekeeping gene encoding a protein that is constitutively expressed and carrying out essential cell functions.

[0049] Methods disclosed herein may include comparing a measured expression level to a reference expression level. The term "reference expression level" refers to a value used as a reference for the values/data obtained from samples obtained from patients. The reference level can be an absolute value, a relative value, a value which has an upper and/or lower limit, a series of values, an average value, a median, a mean value, or a value expressed by reference to a control or reference value. A reference level can be based on the value obtained from an individual sample, such as, for example, a value obtained from a sample from the subject object of study but obtained at a previous point in time. The reference level can be based on a high number of samples, such as the levels obtained in a cohort of subjects having a particular characteristic. The reference level may be defined as the mean level of the patients in the cohort. For example, the reference expression level for a gene or miRNA can be based on the mean expression level of the gene or miRNA obtained from a number of patients who have SNF2 metastases. A reference level can be based on the expression levels of the markers to be compared obtained from samples from subjects who do not have a disease state or a particular phenotype. The person skilled in the art will see that the particular reference expression level can vary depending on the specific method to be performed.

[0050] Some embodiments include determining that a measured expression level is higher than, lower than, increased relative to, decreased relative to, equal to, or within a predetermined amount of a reference expression level. In some embodiments, a higher, lower, increased, or decreased expression level is at least 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 7, 8, 9, 10, 12, 14, 16, 18, 20, 50, 100, 150, 200, 250, 500, or 1000 fold (or any derivable range therein) or at least 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400, 500, 600, 700, 800, or 900% different than the reference level, or any derivable range therein. These values may represent a predetermined threshold level, and some embodiments include determining that the measured expression level is higher by a predetermined amount or lower by a predetermined amount than a reference level. In some embodiments, a level of expression may be qualified as "low" or "high," which indicates the patient expresses a certain gene or miRNA at a level relative to a reference level or a level with a range of reference levels that are determined from multiple samples meeting particular criteria. The level or range of levels in multiple control samples is an example of this. In some embodiments, that certain level or a predetermined threshold value is at, below, or above 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 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, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100 percentile, or any range derivable therein. Moreover, a threshold level may be derived from a cohort of individuals meeting a particular criteria. The number in the cohort may be, be at least, or be at most 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, 250, 260, 270, 280, 290, 300, 310, 320, 330, 340, 350, 360, 370, 380, 390, 400, 410, 420, 430, 440, 441, 450, 460, 470, 480, 490, 500, 510, 520, 530, 540, 550, 560, 570, 580, 590, 600, 700, 800, 900, 1000, 1100, 1200, 1300, 1400, 1500, 1600, 1700, 1800, 1900, 2000 or more (or any range derivable therein). A measured expression level can be considered equal to a reference expression level if it is within a certain amount of the reference expression level, and such amount may be an amount that is predetermined. This can be the case, for example, when a classifier is used to identify the molecular subtype of a metastasis. The predetermined amount may be within 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1.0, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 35, 40, 45, or 50% of the reference level, or any range derivable therein.

[0051] For any comparison of gene or miRNA expression levels to a mean expression levels or a reference expression levels, the comparison is to be made on a gene-by-gene and miRNA-by-miRNA basis. For example, if the expression levels of gene A, gene B, and miRNA X in a patient's metastasis are measured, a comparison to mean expression levels in metastases of a cohort of patients would involve: comparing the expression level of gene A in the patient's metastasis with the mean expression level of gene A in metastases of the cohort of patients, comparing the expression level of gene B in the patient's metastasis with the mean expression level of gene B in metastases of the cohort of patients, and comparing the expression level of miRNA X in the patient's metastasis with the mean expression level of miRNA X in metastases of the cohort of patients. Comparisons that involve determining whether the expression level measured in a patient's metastasis is within a predetermined amount of a mean expression level or reference expression level are similarly done on a gene-by-gene and miRNA-by-miRNA basis, as applicable.

B. IDENTIFYING MOLECULAR SUBTYPES OF METASTASES

[0052] Methods disclosed herein can be used to identify different molecular subtypes of metastatic cancer that correlate with different clinical outcomes and different sensitivities to particular treatment regimens. The subtypes can be identified using an integrated molecular analysis techniques. One such technique described in the Examples below is a similarity network fusion (SNF) algorithm, which incorporates parallel miRNA and mRNA expression networks in a number of patient samples. The SNF analysis established three subtypes of metastatic cancer based solely on expression data, but the subtypes exhibited heterogenous clinical outcomes. Other types of integrated approaches to identifying molecular subtypes can also be used. For example, the inventors analyzed the miRNA and mRNA expression data using consensus clustering of clusters and iClusterPlus and found that, similar to SNF, these approaches identified three distinct subtypes of metastases based on expression alone, and that the distinct subtypes showed statistically significant differences in clinical outcomes of patients. These data demonstrate that the intrinsic subtypes are independent of the type of integrated molecular analysis used to identify them. Furthermore, the discovery that metastatic cancers are heterogeneous and include distinct molecular subtypes enables skilled persons to identify metastatic subtypes of different types of metastatic cancers using integrated analyses of gene and miRNA expression, including liver cancer, testicular cancer, biliary cancer, ovarian cancer, urinary tract cancer, pancreatic cancer, prostate cancer, esophageal cancer, gastric cancer, head and neck cancer, cervical cancer, lung cancer, neuroendocrine cancer, kidney cancer, breast cancer, melanoma, and other cancers that can progress to metastatic cancer.

C. CANCER TREATMENT

[0053] Methods disclosed herein may include administering a cancer therapy or determining a course of cancer treatment based on an identified metastatic subtype. Some embodiments include administering a local cancer treatment or determining that a local cancer treatment is appropriate. Local cancer treatments include those that target cancer tissue using a technique directed to a specific organ or limited area of the body. Local cancer treatments include surgery (i.e., resection), radiation therapy, cryotherapy, laser therapy, topical therapy, high intensity focused ultrasound, and photodynamic therapy. The local treatments may include stereotactic body radiotherapy (SBRT), stereotactic ablative body radiotherapy (SABR), stereotactic radiosurgery (SRS), radiofrequency ablation (RFA), percutaneous cryoablation therapy (PCT), and photodynamic therapy (PDT). The local therapies may be directed at the primary tumor and/or at one or more metastases.

[0054] Systemic cancer therapies are those that are distributed widely within the body, such as a variety of drug treatments, which may be delivered orally or intravenously. Examples of systemic therapies include chemotherapy, hormone therapy, immunotherapy, and targeted therapy (i.e., drugs that are distributed widely within the body, but have targeted effects on cancer cells). More specifically, chemotherapy includes administering drugs such as cyclophosphamide, paclitaxel, epirubicin, methotrexate, gemcitabine, albumin-bound paclitaxel, carboplatin, etoposide, doxorubicin, capecitabine, fluorouracil, vinorelbine, docetaxel, liposomal doxorubicin, eribulin, or irinotecan, including combinations thereof. Immunotherapy includes monoclonal antibodies, such as alemtuzumab, trastuzumab, ibritumomab tiuxetan, brentuximab vedotin, ado-trastuzumab emtansine, denileukin diftitox, and blinatumomab; immune checkpoint inhibitors, such as pembrolizumab, nivolumab, atezolizumab, avelumab, durvalumab, and ipilimumab; and cancer vaccines such as sipuleucel-T.

[0055] Identifying the molecular subtype of metastatic colorectal cancer can be used to determine an appropriate treatment regimen. In some embodiments, the appropriate treatment for SNF1 metastases include EGFR inhibitors, PARP inhibitors, PI3K inhibitors, NOTCH inhibitors, angiogensis inhibitors, DNA damaging agents, STING agonists, innate immune agonists, RNA vaccines, or combinations thereof. In some embodiments, the appropriate treatment for SNF2 metastases include PD-1/PD-L1 immunotherapies, other immunotherapies, beta-secretase inhibitors, lipid-lowering agents, and combinations thereof. In some embodiments, the appropriate treatment for SNF3 metastases include PDGF/PDGFR inhibitors, VEGF/VEGFR inhibitors, angiogenesis inhibitors, JAK1/JAK2 inhibitors, COX2 inhibitors, HDAC inhibitors, DNA demethylating agents, other epigenetic modifiers, and combinations thereof.

[0056] Methods disclosed herein can also include making treatment decisions based on an integrated risk group classification of a patient. This classification combines the molecular subtyping of the metastasis with a clinical risk score of the patient. Integration of SNF subtypes and CRS yielded three prognostic risk groups: (1) low-risk (22% of patients)—SNF1 and SNF2 subtypes with low CRS; (2) intermediate-risk (29% of patients)—SNF2 subtype with high CRS and SNF3 subtype with low CRS; (3) high-risk patients (49% of patients)—SNF1 and SNF3 subtypes with high CRS. A patient's integrated risk group indicates the likelihood of benefit from local metastasis-directed therapies such as surgical resection, stereotactic body radiotherapy (SBRT), stereotactic ablative body radiotherapy (SABR), stereotactic radiosurgery (SRS), radiofrequency ablation (RFA), percutaneous cryoablation therapy (PCT), and photodynamic therapy (PDT): low-risk patients have the highest likelihood of benefit from these therapies, high-risk patients have the lowest likelihood of benefit from these therapies, and intermediate-risk patients have an intermediate likelihood of benefit from these therapies.

[0057] Conventionally, it has been thought that metastatic cancer always requires a systemic therapy. However, the identification of molecular subtypes of metastatic cancer as described herein shows that some metastatic cancers are likely to respond favorably to local therapies and may not need an additional systemic therapy. Conversely, some metastatic cancers are not likely to respond to local therapy alone, or at all, and should therefore be treated with appropriate systemic therapies.

D. EXAMPLES

Example 1. Clinical Characteristics and Patient Outcomes

[0058] One hundred thirty-four patients with comprehensive clinical annotations underwent hepatic resection of limited CRCLM. The clinical characteristics of these patients are summarized in Table 1. The median patient age was 61 years (range, 29-85). Patients were diagnosed with primary adenocarcinoma of the colon (72%) or rectum (28%) and presented with either synchronous (47%) or metachronous (53%) liver metastasis. The initial number of liver metastases was one in 61%, two in 22% and three or more in 17% of patients. Liver metastases were limited to one hepatic lobe in 91% of patients and two hepatic lobes in 9% of patients. Our analysis focused on de novo liver metastases and excluded patients with extrahepatic disease or a history of previously resected metastasis. Patients received uniform treatment with 5-fluorouracil-based perioperative chemotherapy, curative intent management of primary colorectal tumors, and partial hepatectomy of all visible liver metastases (Table 1). Post-operatively all patients were surveilled with serial axial CT imaging and serum CEA levels.

[0059] At a median follow-up of 49 months, 32% of patients had no evidence of metastatic recurrence. These patients had a 10-year OS of 77% whereas patients with clinically evident, recurrent metastases exhibited a 10-year OS of 13% (P<0.0001, log-rank test) (FIG. **1**A). Clinical Risk Scores (CRS), a widely accepted prognostic tool for CRC patients undergoing liver metastasis resection[9,12,13], were calculated using the following adverse clinical and pathological features: (1) disease-free interval between primary tumor diagnosis and development of metastasis <12 months, (2) number of liver metastases >1, (3) largest liver metastasis >5.0 cm, (4) lymph node-positive primary CRC, and (5) CEA>200 ng/mL. 34% of patients exhibited a low CRS (less than two adverse features). As expected, OS was significantly greater for patients with low versus high CRS (two or more adverse features) (10-year: 62% vs. 22%, P=0.0008, log-rank test) (FIG. **1**B). These outcomes were consistent with those previously reported in the literature[9]. In this context, the inventors investigated whether the intrinsic molecular features of CRCLM enhance the identification of patients with long-term survival after hepatic resection of limited metastases.

TABLE 1

Clinical and Pathological Characteristics of Colorectal Cancer Patients with liver metastases selected for study

Clinicopathological Variable	Clinical cohort (n = 134)
Age (median, range)	61 (29-85)
Sex	
Male	57%
Female	43%
Primary tumor	
Colon	72%
Rectum	28%
Metastatic presentation	
Synchronous	47%
Metachronous	53%
Tumor size	
<=5 cm	78%
>5 cm	22%
Primary lymph node status	
Negative	36%
Positive	64%
Initial number of liver metastases	
1	61%
2	22%
3+	17%
Disease-free interval from primary tumor to metastasis	
<12 mo	61%
>=12 mo	39%
CEA level	
<200 ng/mL	95%
>=200 ng/mL	5%
Clinical Risk Scores (CRS)	
<2	34%
≥2	66%
Hepatic involvement	
Unilobar	91%
Bilobar	9%
Extent of resection	
Wedge/segmentectomy	58%
Lobectomy/ extended lobectomy	42%
Resection margin	
Negative	85%
Positive	15%
Peri-operative chemotherapy	98%
Follow-up (mo) (median, range)	49 (4 · 3-328)
Metastatic recurrence	68%
Patterns of failure	
Liver only	38%
Liver and lung	34%
Other sites (e.g. peritoneum, bone, adrenal, brain)	28%
Death event	58%

Example 2. Consensus Molecular Subtypes of Primary Colorectal Cancer

[0060] Gene expression analysis is an established approach for molecular subtyping of primary human cancers[14,15]. The International Colorectal Cancer Subtyping

Consortium (CRCSC) demonstrated the existence of four biologically and clinically distinct Consensus Molecular Subtypes (CMS) of CRC based on gene expression analysis of 3,962 primary tumors[16,17]. However, it is unknown whether CMS subtypes also exist in CRCLM. First, the application of CMS classification to the analysis of RNA Sequencing data from 558 primary CRC tumors in The Cancer Genome Atlas (TCGA)[18] was validated, which verified the expected frequencies of CMS subtypes (FIG. **2**A). Then the single-sample CMS classifier was applied to the analysis of two independent CRCLM datasets derived from RNA Sequencing analysis of 93 patients in our study (Cohorts UC and NS in FIG. **2**A), which demonstrated CMS2 and CMS4 patterns in 62% and 12% of liver metastases with a notable absence of CMS1 (1%) and CMS3 (0%) patterns (FIG. **2**A). The inventors examined whether this result was related to selection bias for patients with limited, resectable metastatic disease or was generalizable to widely metastatic or unresectable CRCLM. In five independent datasets comprising an additional 234 CRCLMs derived from either hepatic resection (60% of samples) or biopsy due to unresectable or widely metastatic disease (40% of samples), similar frequencies of CMS2 and CMS4 patterns in 60% and 7% (vs. 37% and 23% of primary CRC) were observed. CMS1 and CMS3 subtypes comprised 2% and 1% of liver metastases (vs. 14% and 13% of primary CRC). In addition, 30% of CRCLM were unclassifiable based on CMS subtypes (FIG. **2**A). While CMS classes were associated with distinct clinical outcomes in primary CRCs, no association between CMS subtypes and OS in patients with resected liver metastases was observed (FIG. **6**).

Example 3—Integrated Transcriptional Subtypes of Colorectal Liver Metastasis

[0061] Transcriptomic analyses of individual mRNA or miRNA datasets were limited in the molecular subtyping of colorectal liver metastases (FIGS. **7** and **8**). Based on previous work which demonstrated coordinated miRNA-mRNA transcriptional networks underlying metastatic phenotypes, as well as primary CRC subtypes[19-22], an integrated expression analysis was performed to uncover novel intrinsic subtypes of CRCLM. The Similarity Network Fusion (SNF) algorithm was utilized to incorporate parallel miRNA and mRNA networks in 93 patient samples independently of clinical, pathological, or survival data. SNF is a computational method for integration of diverse types of data with superior performance in the identification of cancer subtypes when compared to single data and established integrative approaches[23]. Three distinct molecular subtypes of CRCLM were observed, denoted SNF1 (33%), SNF2 (28%), and SNF3 (39%) (FIG. **2**B). Despite the detection of SNF subtypes solely based on molecular features, the inventors found the SNF subtypes exhibited heterogeneous clinical outcomes with 10-year OS of 37%, 64%, and 20%, respectively (P=0.021, log-rank test) (FIG. **2**C and FIG. **10**). Using permutation analysis, they examined the importance of the SNF cluster structure on its association with OS. After 1,000 randomized mRNA-miRNA permutations, they found that the SNF clustering algorithm was unlikely to generate our empirical OS difference by chance (P=0.0007) (FIG. **11**). Importantly, patients with SNF2 metastases experienced fewer metastatic recurrences or deaths after hepatic resection as compared to SNF1 or SNF3 metastases (FIG. **2**D and FIG. **12**), and metastatic recurrences of SNF2 metastases were significantly more likely to be limited in number, defined as 1-3 subsequent metastases, as compared to SNF1 or SNF3 metastases (FIG. **2**D).

[0062] Each SNF subtype demonstrated distinct patterns of mRNA and miRNA expressions (FIG. **2**E). SNF2 and SNF3 metastases displayed similar patterns of primary CRC CMS subtypes whereas, by contrast, SNF1 metastases almost exclusively exhibited the CMS2 pattern (FIG. **13**). However, only 10%, 5.6%, and 16% of SNF1-, SNF2-, and SNF3-specific gene sets overlapped with the CMS classifier suggesting that SNF subtyping provided independent classification of CRC tumors. In addition, the type of perioperative chemotherapy had no effect on the molecular patterns (FIG. **14**) or overall survival of resected CRCLM. Given that independent datasets of integrated molecular data do not exists for clinically annotated CRCLM, the inventors trained and validated an mRNA-based classifier to identify SNF2 patients. They found that the molecular classifier accurately identified SNF2 patients with 100% sensitivity and 81% specificity in their patient cohort (FIGS. **15**A and **15**B). In an independent dataset of CRCLM patients with similar clinical and pathological features treated with hepatic resection at the Memorial Sloan-Kettering Cancer Center (n=96), metastases classified as the SNF2 subtype were confirmed to demonstrate favorable clinical outcomes as compared to metastases with SNF1 or SNF3 patterns (FIG. **15**C). These findings supported SNF subtypes and their associations with clinical outcomes in an independent dataset from a distinct institution.

Example 4—Molecular Characterization of Intrinsic Liver Metastasis Subtypes

[0063] Ensemble of Gene Set Enrichment Analyses (EGSEA) provided substantial insight into the biological features of SNF subtypes (FIG. **3**A). EGSEA quantifies the enrichment of biologically defined gene sets within a gene expression profile[24]. SNF3 metastases were found to show enrichment for expression patterns associated with high stromal infiltration, epithelial-mesenchymal transition (EMT), extracellular matrix remodeling, angiogenesis, inflammatory response, and KRAS signaling (FIG. **3**A). SNF2 metastases similarly exhibited enrichment for EMT and KRAS pathways; however, SNF2 metastases were distinguished by high immune infiltration, enrichment of interferon alpha and gamma signatures, and activation of p53 pathways. In concert with these findings, SNF2 metastases significantly overexpressed innate and adaptive immune genes, such as those which mediate T cell activation and crosstalk between antigen presenting cells and T cells, as compared to SNF1 and SNF3 metastases (FIG. **3**B and Table 7). SNF1 metastases displayed both low stromal and low immune infiltration signatures but were markedly enriched for E2F/MYC signaling, including TERT (telomerase) overexpression, as well as abnormalities in DNA damage signaling and cell cycle checkpoints.

[0064] Importantly, CRCLM subtypes were also discernible at the histological level (FIG. **16**). SNF2 metastases exhibited dense band-like peritumoral infiltration of CD3-positive and CD8-positive lymphocytes extending intratumorally, and trichrome staining demonstrated minimal fibrosis, whereas SNF3 metastases were distinguished by marked intratumoral and peritumoral fibrosis which harbored peritumorally restricted lymphocytic infiltrate. In contrast, SNF1 metastases revealed prominent nests of tumor cells with minimal CD3-positive or CD8-positive cells or fibrosis. These findings demonstrated unique molecular properties of SNF subtypes associate with differential patient outcomes after hepatic resection of limited CRCLM.

Example 5—Mutational and Copy Number Landscapes

[0065] Fifty-nine liver metastases and matched normal liver specimens underwent next-generation genomic sequencing using OncoPlus, a clinically validated hybrid capture genomic sequencing platform comprising 1,212 commonly altered cancer genes for mutational and copy number analyses[11]. Mutation Significance (MutSig) analysis confirmed enrichment in CRC driver gene mutations of APC, TP53, KRAS, PIK3CA, SOX9, SMAD4, and FBXW7 in 83%, 73%, 37%, 20%, 14%, 14% and 12% of liver metastases, respectively (FIG. **3**C, FIG. **17**, and Table 8). In addition, the inventors observed frequent gene-level copy number variations, including amplifications of VEGFA (FIG. **3**C), MYC, and ERBB2 and deletion of MAP2K4, which were previously described for primary CRC[18]. They also found that mutational patterns reflected the anatomic location of the primary tumor origin of liver metastases. Eighty-three percent of liver metastases from right-sided colon cancers exhibited activating somatic mutations in KRAS, in contrast to 24% from left-sided cancers (P=0.0005, Fisher's exact test). Also, PIK3CA mutations occurred in 50% of metastases derived from right-sided primary tumors versus 8% from left-sided primary tumors (P=0.0038, Fisher's exact test).

[0066] These findings were extended by characterizing the mutational and copy number landscapes of CRCLM by SNF subtype. Unique somatic mutations in each SNF subtype were identified (FIG. **3**D and Table 9). SNF3 metastases demonstrated exclusive somatic mutations in SMAD3, whereas NOTCH1 and PIK3C2B mutations occurred only in SNF1. By contrast, NRAS, CDK12, and EBF1 mutations were unique to SNF2 metastases (FIG. **3**D). In addition, amplification of VEGFA was more prevalent in SNF1 and SNF3 metastases as compared to SNF2 metastases (FIG. **3**D and Table 9). Notably, no significant differences were found in the frequency of KRAS or BRAF mutations across SNF subtypes. Taken together, these data support the notion that SNF subtypes of CRCLM harbor distinct genomic aberrations.

[0067] Furthermore, the inventors found that the median number of mutations per sample was not statistically different across SNF subtypes. Given that mismatch repair deficiency leading to microsatellite instability (MSI) contributes to tumor hypermutation in association with cytotoxic immune infiltration[25], the inventors investigated whether MSI explained the SNF2 subtype. They identified an MSI phenotype in 3.4% of patients, which is consistent with the incidence of MSI in metastatic colorectal cancer[26]. However, only one SNF2 metastasis demonstrated an MSI-high phenotype, while two metastases—one from SNF1 and one from SNF2, exhibited an MSI-low phenotype. The SNF2 MSI-high and MSI-low metastases, but not SNF1 MSI-low metastasis, showed significant enrichment of cytotoxic cell signature expression (FIG. **18**). Although mutational burden did not correspond to the SNF2 immune subtype, increased mutational burden associated with MSI in SNF2, including hypermutation (n=1,760 mutations) in the MSI-low metastasis related to POLE mutation. In addition, recent data suggest that specific mutations also predict cytotoxic immune responses[27]. In this regard, ARID2 mutations are associated with increased cytolytic activity in multiple types of cancers. In the inventor's dataset, a significant elevation in cytotoxic immune responses in patients with somatic ARID2 mutations was found (FIG. **18**). As well, metastases with SNF2-specific mutations in CDK12, NRAS, or EBF1, in contrast to metastases with SNF1- or SNF3-specific mutations in NOTCH1, PIK3C2B, or SMAD3, showed significant enrichment for cytotoxic immune responses (P=0034). Taken together, these findings identify novel mutations associated with immune responses and favorable clinical outcomes of CRCLM.

Example 6—Integrated Risk Stratification

[0068] The inventors investigated whether SNF molecular subtyping could improve clinical risk stratification after hepatic resection of CRCLM by augmenting the prognostic effect of CRS. Multivariate Cox proportional hazard analysis indicated the prognostic impact of SNF subtypes was statistically independent of but complementary to CRS (FIG. **19**). Integration of SNF subtypes and CRS yielded three prognostic risk groups: (1) low-risk (22% of patients)—SNF1 and SNF2 subtypes with low CRS; (2) intermediate-risk (29% of patients)—SNF2 subtype with high CRS and SNF3 subtype with low CRS; (3) high-risk patients (49% of patients)—SNF1 and SNF3 subtypes with high CRS (FIG. **4**A and FIG. **19**). Multivariate Cox proportional hazard analyses incorporating primary tumor anatomic site, type of perioperative chemotherapy, treatment year, or mutational data, including KRAS mutation, BRAF mutation, or MSI, did not independently contribute to prognostication in our cohort. Ten-year OS for low-, intermediate-, and high-risk groups were 94%, 45%, and 19%, respectively, at median follow-up times of 76, 54, and 40 months (FIG. **4**A). Notably, while SNF1 metastases generally demonstrated unfavorable clinical outcomes, a subset of SNF1 metastases with low CRS (23%) achieved long-term survival, which correlated with a reduced frequency of extrahepatic metastatic recurrence in these patients in contrast to SNF1 metastases with high CRS (33% vs. 81%). While distant metastasis-free survival significantly differed across risk groups (median value—low-risk: 59 mo. vs. intermediate-risk: 35 mo. vs. high-risk: 13 mo; P=0.0021) (FIG. **20**A), 47% of low-risk, 68% of intermediate-risk, and 86% of high-risk patients developed subsequent metastatic recurrence after hepatic resection (FIG. **20**B). Importantly, metastatic recurrences were limited in number in 100% of low-risk patients in contrast to 87% of intermediate-risk and 34% of high-risk patients (FIG. **4**B) (P<0.0001, Chi-square test across groups). These findings demonstrate SNF subtypes of CRCLM significantly improve clinical risk stratification for the identification of patients with favorable prognoses after hepatic resection of limited de novo CRCLM.

Example 7—Methodology

[0069] Patients: Samples from 134 adults with liver metastases from primary CRC of which 121 metastases from independent patients successfully underwent molecular analysis were analyzed (FIG. **5**). The characteristics of these patients are described in Table 1, Table 2, and the Example 7. The inventors utilized a retrospective clinical cohort study design to identify patients who received uniform treatment for limited (defined as 1-5 lesions involving one or both hepatic lobes), resectable de novo CRC liver metastasis (CRCLM) at two collaborating institutions. Appropriate consent from Institutional Review Boards at each respective cancer center was obtained.

[0070] Analytic Platforms: microRNA (miRNA) profiling for 116 samples using Affymetrix miRNA 4.0 Arrays was performed as well as whole genome RNA sequencing for 95 samples using Illumina TruSeq Stranded Total RNA Sequencing. In addition, hybrid capture genomic sequencing of liver metastases and matched normal liver specimens from 59 patients using the OncoPlus panel was performed[11]. All sequencing was conducted on Illumina HiSeq sequencers. Also performed was microsatellite instability (MSI) analysis on 89 samples using the Promega MSI 1.2 clinical assay according to FDA approved guidelines. Clinical data were frozen on Apr. 30, 2016 and molecular data were frozen on Jun. 26, 2016. Overall survival (OS), defined as the interval between hepatic resection and death from any cause or until censoring at the time the patient was last known to be alive, was chosen as the optimal primary endpoint. The complete list of datasets is provided in Table 2.

[0071] Statistical analysis: The statistical analysis included Fisher's exact tests for associations of categorical variables when there were two categories or Chi-square tests when there were three categories. Kaplan-Meier and Cox proportional hazard analyses were used to examine the associations of molecular features with clinical outcomes. Multiple testing corrections were performed using the Benjamini-Hochberg method. All reported P-values are two-sided. A complete description of the methods is in the methods described hereafter.

Clinical Information

1. Patient Characteristics

[0072] A retrospective clinical cohort study was conducted on patients who underwent hepatic resection of histologically confirmed metastatic colorectal adenocarcinoma at the University of Chicago Medical Center (Chicago, Ill.) and NorthShore University Health System (Evanston, Ill.) between 1994 and 2012. During this time period, approximately 60-75 patients per year underwent hepatic resection of colorectal liver metastases at the two participating institutions. All available clinical, pathologic, radiologic, and outcome data were collected for patients using medical records. Patients with unresectable or extrahepatic disease at the time of metastatic diagnosis were excluded from this study. In total, 134 consecutive patients with metastatic colorectal cancer who underwent surgical resection of limited de novo liver metastases were selected for molecular analysis. Patients were uniformly treated with perioperative chemotherapy, definitive treatment of primary colorectal cancer, and partial hepatectomy for resection of liver metastases. Detailed cohort characteristics are provided in Table 1 and Table 2. This study was approved by the Institutional Review Boards at each respective institution. Dates of recurrence, death or last follow-up were extracted from medical records and Social Security Death databases. Clinical risk scores (CRS) were calculated as previously described[1].

2. Pathologic Examination

[0073] Formalin-fixed paraffin-embedded (FFPE) specimens were collected from archived pathologic tissue. FFPE specimens were catalogued and histologically reviewed by an expert pathologist (Dr. Nora Joseph) to ensure adequacy of the specimen and histologic quality control. Tissue blocks containing sufficient tumor tissue were subjected to 2 mm punch biopsies of both tumor and normal liver regions. For each surgical specimen, representative FFPE tissue blocks and corresponding H&E slides were analyzed to confirm the diagnosis of colorectal adenocarcinoma and identify regions containing high quantities of viable tumor cells, as well as independent regions containing normal liver parenchyma. Three cores from tumor and normal tissue regions were obtained. For each specimen, all three cores were combined to reduce intratumoral variability. This procedure was repeated for both tumor and normal biopsies for each patient.

[0074] Nucleic Acid Extraction

[0075] Punch biopsy specimens were deparaffinized and processed using the RecoverAll Total Nucleic Acid Isolation Kit (Ambion, TX) according to the manufacturer's instructions. Briefly, 200 μL of digestion buffer and 4 μL of protease were added to each sample and incubated overnight at 55° C. RNA and DNA were extracted following the RecoverAll protocol according to the manufacturer's recommendations. Nucleic acid quantification was performed using a NanoDrop 1000 Spectrophotometer and a Qubit® Fluorometer. Nucleic acid extracts were stored at −80° C. until further analysis.

[0076] RNA Sequencing

[0077] 1. Library Construction: RNA integrity and quantity were evaluated using an Agilent 2100 Bioanalyzer (Agilent Technologies, CA). Reverse-stranded paired-end 75 base-pair sequencing libraries were constructed using Illumina Total RNA Stranded Kits. Ribosomal RNAs (rRNAs) were depleted by using the Ribo-Zero rRNA Removal Kit (Illumina). Libraries were sequenced on a HiSEQ2500 machine using standard reagents and protocols provided by Illumina. In total, 95 metastatic samples were successfully sequenced using this approach.

[0078] 2. Read Alignment and Quantification: Unless otherwise specified, all data analyses were performed under the R programming and software environment for statistical computing and graphics version 3.3 (R Core Team, 2016). FastQ files for each sample were assessed for quality using the FastQC tool (version 0.11.2). Raw reads were aligned to the GRCh38 primary genome assembly using Spliced Transcripts Alignment to a Reference (STAR) aligner (version 2.4.2a) 1-pass algorithm[2]. After sorting the bam files in lexicographical order with the sambamba program[3], the inventors assigned the reads to exon features annotated in GENCODE (release 22) using the FeatureCounts tool from the subread package (version 1.4.6) and summarized the read counts by genes[4]. The post-alignment quality control was carried out with Picard tools (version 1.117) and RSeQC package (version 2.3.1). Specifically, the inventors examined the QC data regarding the alignment summary, gene body coverage, read distribution, and ribosomal RNA depletion rate.

[0079] 3. Data Normalization: The inventors used functions in the R/Bioconductor package edgeR to extract the raw counts of the reads that were mapped to the protein-coding genes[5]. After removing the genes with zero read counts across all samples, the inventors calculated the normalization factors to scale the raw library sizes and the log 2-transformed count per million (log-CPM) for the expression level of each gene. The log-CPM values were corrected for batch effect (sequencing lane effect and institution) using removeBatchEffect function from the R/Bioconductor package limma[6]. 18,714 genes were retained for the subsequent analyses.

[0080] 4. Detection of Differentially Expressed mRNAs: To identify differentially expressed mRNAs among samples grouped by Similarity Network Fusion (SNF—see Example 7, Similarity Network Fusion) clusters, the inventors first removed non/low-expressed genes in comparison groups by requiring read counts to be at least 1 across a minimum number of samples in one of the comparison groups, followed by trimmed mean of M-values (TMM) normalization using the calcNormFactors function in the edgeR package. Next, the inventors removed heteroscedascity from the count data using the voomWithQualityWeights function from the limma package with quantile normalization method enabled. The inventors then fit a linear model for each gene using the limma algorithm, adjusted for batch effect, and ranked the genes for differential expression using the empirical Bayes method with trend and robust options enabled. The differentially expressed genes were identified with the Benjamini-Hochberg procedure for multiple test adjustment and fold-change. The adjusted P-value threshold and fold-change threshold were set at 0.05 and 2.0, respectively (Tables 3A-C).

[0081] microRNA Expression Profiling

[0082] RNA integrity and quantity were evaluated using an Agilent 2100 Bioanalyzer (Agilent Technologies, CA). Total RNA (500 ng) was processed for biotin labeling according to the Affymetrix Flash Tag Biotin HSR RNA labeling guide (Affymetrix, CA). The biotin-labeled target was hybridized to Affymetrix miRNA 4.0 Array Chips for 16h at 48° C. and 60 rpm in an Affymetrix 640 hybridization oven. Arrays were washed and stained in an Affymetrix Fluidics Station 450 according to the Affymetrix GeneChip expression guide. The arrays were scanned using the Affymetrix GeneChip Scanner 3000 7G. CEL intensity files were generated using GCOS software. In total, 116 metastatic samples were successfully assayed using this approach.

[0083] 1. Data Pre-Processing and Normalization: The methods used in this analysis are available as part of the R/Bioconductor packages affy, oligo, limma and sva[6,7]. The raw Affymetrix GeneChip miRNA 4.0 Array CEL files were imported to R using the read.celfiles function from the oligo package. The inventors first performed robust normexp-by-control background correction using the nec function from the limma package with the robust option enabled[8]. They then normalized the log 2-transformed expression data using cyclic loess normalization with the array weight method. Finally, the inventors summarized the probes into probesets using the rma function from the affy package with the options normalize and background disabled. To remove batch effects caused by array processing dates and the patient cohorts, they applied the ComBat algorithm implemented in the sva package[9]. Two batch factors: (1) institution and (2) microarray scan date were considered. A single sample was run in batch 6 and combined with samples from batch 5. The inventors removed non/low-expressed probesets and retained the probesets representing 778 mature human miRNAs for the subsequent analyses.

[0084] 2. Detection of Differentially Expressed miRNAs

[0085] The inventors applied the limma method to identify differentially expressed miRNAs among the samples grouped by SNF clusters. They first estimated the relative quality weights for each array using the arrayWeightsSimple function, and then fit a linear model for each probeset adjusted for batch effect, followed by ranking probesets for differential expression using empirical Bayes method. The differentially expressed miRNAs were identified with the Benjamini-Hochberg procedure for multiple test adjustment and fold-change. The adjusted P-value threshold and fold-change threshold were set at 0.05 and 2.0, respectively (Tables 4A-C).

[0086] Consensus Clustering of Expression Data

[0087] Unsupervised consensus clustering analysis was performed on independent mRNA and miRNA expression data sets using the R package ConsensusClusterPlus (version 1.38.0). The inventors selected the most informative mRNAs or miRNAs for clustering, which consisted of the top 25% most variable mRNAs or miRNAs, as measured by the median absolute deviation (MAD). Normalized expression data from previous procedures were first standardized using the data normalization function in the R package clusterSim (version 0.45-1). To run ConsensusClusterPlus, the inventors preset the options as a maximum evaluated cluster k=66, 80% samples per resampling, 1,000 resamplings, Euclidean distance, and k-means clustering algorithm. They chose complete and average linkage as the inner-linkage and final linkage, respectively. The optimal number of k clusters was inferred by inspecting the consensus cumulative distribution function (CDF) plot and the proportion of ambiguously clustered pairs (PAC) plot where the optimal k corresponds to the lowest PAC[10] (k=2, FIGS. **7** and **8**).

[0088] Consensus Molecular Subtyping (CMS) of Colorectal Liver Metastases.

[0089] Microarray expression data derived from 183 patients with colorectal liver metastasis were collected from ArrayExpress (study IDs: E-MTAB-1951, E-GEOD-62322, E-GEOD-41258, and E-GEOD-35834). Study E-MTAB-1951 contains 96 samples profiled on the Illumina HumanHT-12 v3.0 Expression BeadChip. E-GEOD-62322 and E-GEOD-41258 contain 19 and 47 samples that were profiled on Affymetrix HG-U133A Arrays, respectively. E-GEOD-35834 consists of 27 samples profiled on the Affymetrix Human Exon 1.0 ST Array. The inventors also used two sets of normalized RNA Sequencing data. One cohort includes 93 metastases from our cohort which were reanalyzed with RSEM to assess TPM abundances, while the other cohort contains 45 liver metastases that were obtained from the Memorial Sloan-Kettering Cancer Center and processed similar to previously described methods in Example 7 (RNA sequencing). For E-MTAB-1951, raw expression data was preprocessed with variance stabilizing transformation and quantile normalization using the lumi package (version 2.26.3). For the remaining microarray studies, CEL files were downloaded directly from ArrayExpress and processed with fRMA (version 1.28.0) for core annotation targets summarized by robust weighted average. Level 3 TCGA READ and COAD RNA Sequencing RSEM expression data was obtained from Sage-Bionetworks Synapse repository (syn: syn2320098, syn2320092, syn2320147, and syn2320079). TPM expression data corresponding to primary tumor samples were selected, offset by 1, and log 2 transformed. Multiple gene level mappings were resolved by singular value decomposition. Datasets from both tissues were merged, and a custom ComBat correction was performed to account for batch effects between HiSeq-RNASeqV2 and Illumina-GA platforms. All scripting and normalization methods are available for download via the CRC Subtyping Consortium's github including the merging protocol (https://github. com/S age-Bionetworks/crcsc/blob/dc58542555e281c1ccb55aeb73 d087e7d0bdf6bf/groups/G/dataQc/tcgaCrcRNAseq-merged.R) and miscellaneous normalization procedures (https://github.com/Sage-Bionetworks/crcsc/blob/dc58542555e281c1ccb55aeb73 d087e7d0bdf6bf/groups/G/dataQcaGnorm.R).

[0090] For both microarray and RNA Sequencing expression data, features were mapped to corresponding Entrez gene IDs using annotation sets provided by Ensembl GRCH38 and Bioconductor including hgu133a.db (version 3.2.3), huex10sttranscriptcluster.db (version 8.6.0), lumiHumanIDMapping (version 1.10.1), or org.Hs.eg.db (version 3.3.0). For multiple annotations mapping to a unique gene feature, either the median probeset value or the largest coefficient of variation across RNAseq samples was retained as an expression estimate for the corresponding gene feature. CMS classification was performed using the single sample procedure (SPP) (https://github.com/Sage-Bionetworks/CMSclassifier).

[0091] Similarity Network Fusion

[0092] The matched normalized mRNA and miRNA expression data of 93 metastases were first separately standardized using the standardNormalization function from the R package SNFtool (version 2.2). The Euclidean distances between all pairs of samples in mRNA and miRNA data were calculated, respectively. An affinity matrix was computed using the function affinityMatrix with the number of nearest neighbors K and the variance for local model alpha. The inventors then performed similarity network fusion on affinity matrices of mRNA and miRNA with the number of iterations T, which was used in the subsequent spectral clustering step where samples were assigned to one of the SNF clusters. Three clusters were identified using default settings. In order to find other possible compositions of three clusters, the inventors tested 168 parameter combinations of K (10, 15, 20, 25, 30, 35, 40), alpha (0.3, 0.4, 0.5, 0.6, 0.7, 0.8), and T (20, 30, 40, 50). For each parameter setting, they applied the estimateNumberOfClustersGivenGraph function to estimate the possible number of clusters using two heuristic methods: (1) eigen gap and (2) rotation cost. The inventors retained the clustering results which comprised three clusters and calculated the median Silhouette index (SI) of each result. The top 8 clustering results that had the highest median SIs were selected (FIG. **9**). A majority voting scheme was applied to determine the final cluster membership based on the top 8 clustering results. In the event of a tie, the inventors chose the membership defined by four clustering results with the largest median Sis.

[0093] Robustness of SNF Clustering on Overall Survival Previous work has shown that the SNF algorithm for clustering is statistically robust[11]. The inventors examined whether the observed survival difference between SNF clusters could be reproduced by random chance. To this end, they performed permutation analyses. For each permutation, miRNA profiles were shuffled and randomly assigned to mRNA profiles. Subsequently, SNF clustering was performed de novo and each patient was assigned to one of three resulting groups. Differential overall survival across clusters was then assessed with a log-rank test. This process was repeated 1,000 times, and log-rank p-values were used to construct a null distribution. The inventors examined the number of instances when p-values from the null distribution were more extreme (i.e. smaller) than the empirical p-value (FIG. **11**).

[0094] Ensemble of Gene Set Enrichment Analyses (EGSEA).

[0095] Raw gene feature counts were mapped to Entrez ID using the R/Bioconductor package org.Hs.eg.db v3.4.0[5]. Low/non-expressed genes with less than 1 CPM across the minimum number of samples in any SNF group were excluded from subsequent analysis using edgeR v3.16.5. Quality weighted, quantile, and log-normalized CPM were calculated using limma-voom v3.30.11. Gene set enrichment was performed using the R/Bioconductor package EGSEA v1.2.0[12] with planned contrasts of each SNF group against the average of the remaining groups. Independent EGSEA analyses were performed for gene lists provided by MSigDB v5.2[13] (Tables 5A-C) and a custom gene list identifying numerous immunological, canonical, and metabolic pathways[14] (Tables 6A-C). Intratumoral immunome profiling was performed as previously described[15], and resulting gene lists were used to calculate SNF-level and single sample enrichment scores using EGSEA.

[0096] SNF Class Predictor

[0097] Data Preprocessing: To build a classifier to distinguish samples between SNF cluster 2 (C2) and SNF cluster 1 and 3 combined (C13), the normalized mRNA expression data of 93 patients was split into a training set, consisting of 20 SNF cluster 2 samples and 51 cluster 1 and 3 samples, and a test set, consisting of 6 cluster 2 samples and 16 cluster 1 and 3 samples. The class ratio remained unchanged during the partition. For the training set, the inventors first filtered genes with near zero-variance. They then identified highly correlated genes with a pair-wise absolute correlation coefficient greater than 0.7, and removed those with the largest mean absolute correlation. They further removed potential linear dependencies of the data using the findLinearCombos function from the R package Caret (version 6.0). They applied the preProcess function to center and scale the training and test data by mean and standard deviation, followed by rescaling data to −1 and 1.

[0098] Model Training and Testing: The inventors applied Prediction Analysis of Microarrays (PAMR, version 1.55)—a nearest shrunken centroid classification algorithm—on the training set[16]. A 10-fold cross-validation was performed to obtain the optimal threshold of 2.72 for the prediction, where the overall error rate was 0.056. The final classification model contains 113 genes (Tables 10A-C) and was evaluated using the held-out test data of 6 SNF cluster 2 samples and 16 SNF cluster 1 and 3 samples. Performance metrics such as accuracy, balanced accuracy, sensitivity, specificity, positive prediction value (PPV), negative prediction value (NPV), Cohen's Kappa, Matthew's correlation coefficient, and area under the curve (AUC) were calculated using the confusionMatrix function from the Caret package and an in-house script (FIG. **15**A and FIG. **15**B). A nearest shrunken centroid classification algorithm was also used to generate a classification model to identify SNF2 metastases based on miRNA expression. This classification model contains 53 miRNAs (Tables 11A-C).

[0099] Independent Validation of Classifier: The inventors downloaded the raw expression data of 96 patients from ArrayExpress (study ID: E-MTAB-1951). They prioritized the analysis of the E-MTAB-1951 samples as it is the only publicly available colorectal cancer liver metastasis dataset with available clinical annotations (i.e. Clinical Risk Scores (CRS)) to test for association with SNF membership grouping. The samples were profiled using the Illumina HumanHT-12 v3.0 Expression BeadChip. Using the R/Bioconductor package lumi (version 2.26.4)[17], they transformed the expression data via variance-stabilizing transformation (VST) algorithm, followed by between-chip normalization with the robust spline normalization (RSN) algorithm. For multiple probes that mapped to the same Ensembl gene ID, they removed those with the smallest variance across samples. The inventors re-trained the PAM classifier on all 93 samples in our cohort using the 113 genes selected from the previous analysis and applied it to the normalized E-MTAB-1951 microarray data set. For genes that were missing in the microarray data, they replaced the expression values with −1 after scaling the data to −1 and 1. The concordance between the predicted SNF clustering memberships and the Clinical Risk Scores (CRS) from the E-MTAB-1951 samples was examined using contingency analysis (FIG. **15**C).

[0100] Hybrid Capture Next Generation Sequencing

[0101] Targeted Capture Sequencing Panel: For each specimen, DNA from 1,212 exonic regions was captured using the UCM-OncoPlus panel based on the NimbleGen SeqCap EZ custom capture method as previously described[18]. In brief, this approach utilizes a tiered assay system in which highly clinically relevant genes (tier 1, n=316) are sequenced approximately 3-fold deeper than the remaining (tier 2) genes. Capture libraries were generated using the Illumina TruSeq platform. Libraries were multiplexed with 6 base-paired indexes up to 9 samples per lane and sequenced using Illumina HiSeq2000 and HiSeq2500 machines. FastQ files were generated using Illumina's BCL2FastQ1.8.4.

[0102] Sequencing Data Alignment: FastQ files were quality trimmed using cutadapt v1.9.1 (http://cutadapt.readthedocs.io/en/stable/guide.html) for Phred score quality on 3' end Q>=30[18] and a minimum length of 19 after trimming (bwa-mem recommended minimum read size). Remaining reads were aligned using the bwa-mem algorithm v0.7.8 (http://bio-bwa.sourceforge.net) against the hg19 reference. PCR duplicates were removed by Broad Institute Picard tools v1.128 MarkDuplicates (https://github.com/broadinstitute/picard). Bedtools v2.22.1 (http://bedtools.readthedocs.io/en/latest/) was used to ascertain coverage at tier 1 and tier 2 loci. Samples that did not have a mean 300× depth of coverage at tier 1 genes were excluded from subsequent analyses. In targeted-capture sequencing, oxidative damage can be pervasive and lead to false positive variant calls at sites with sequence context CCG being read as CAG[19]. Sample-level oxidative damage was calculated using Picard CollectOxoGMetrics. Sample with ArtQ[19] scores less than 21 were removed. Overall, 59 unique metastasis-normal pairs were available for analysis.

[0103] Example alignment pipeline flow:

[0104] 1. cutadapt -m 19 --quality-base=33 -q30 -a ZZZ-A ZZZ -o sample_filtered_r1.fastq.gz -p sample_filtered_r2.fastq.gz sample_r1.fastq.gz sample_r2.fastq.gz>>sample.cutadapt.log 2>> sample.cutadapt.log

[0105] 2. bwa mem -t 8 -R "@RG\tID: sample flowcell id\tLB: sample\tSM: sample\tPL:illumina"-v 2 hg19.fa sample_filtered_r1.fastq.gz sample_filtered_r2.fastq.gz|samtools view -bT hg19.fa ->sample.bam)>sample.bwa.pe.log 2>&1

[0106] 3. novosort -c 8 -m 30G --tmpdir novosort_tmp -o sample.srt.bam -i sample.bam>sample.novosort.log 2>&1

[0107] 4. java -Xmx30g -jar picardjar MarkDuplicates CREATE INDEX=true TMP_DIR=picard_tmp REMOVE_DUPLICATES=true ASSUME_SORTED=true MAX_FILE_HANDLES_FOR_READ_ENDS_MAP=500 INPUT=sample. srt.bam OUTPUT=sample.rmdupsrt.bam METRICS_FILE=sample.rmdupsrt.metrics VALIDATION_STRINGENCY=LENIENT>sample.picard.rmdup.pe.log 2>&1

[0108] 5. bedtools coverage -hist -abam sample.rmdup.srt.bam -b capture_panel_v3_t1.bed|grep all>sample.capture_t1.hist

[0109] 6. bedtools coverage -hist -abam sample.rmdup.srt.bam -b capture_panel_v3_t2.bed|grep all>sample.capture_t2.hist

[0110] 7. java -Xmx30g -jar picardjar CollectOxoGMetrics I=sample.rmdup.srt.bam O=sample.oxo_summary.txt R=hg19.fa INTERVALS=capture_panel_v3.intvl 2>sample.oxo.log;

[0111] Variant Calling and Filtering: Single nucleotide variants (SNVs) were called using MuTect v1.1.7 (http://archive.broadinstitute.org/cancer/cga/mutect). Insertions and deletions (indels) were called using scalpel-discovery 0.5.3 (http://scalpel.sourceforge.net/). Calls not annotated as "PASS" or "KEPT" were removed. For both SNVs and indels, only calls falling within genomic coordinates targeted by the capture panel were retained for subsequent analyses. Targeted capture libraries have been shown to be susceptible to oxidative damage. Even samples that do not have pervasive oxidative damage can have false positive calls attributable to this phenomenon[19]. All SNV calls were assigned a FoxoG score using metalfox (https://github.com/cpwardell/bin/blob/master/metalfox.py). Based on previously reported studies[19], calls without a MuTect tumor_lod greater than −10+(100/3) * FoxoG were removed as they were likely a consequence of oxidative damage. All variants were annotated using snpeff v3.6c (http://snpeff.sourceforge.net/), hg19 reference. Only variants that exist within coding regions or disrupted splice sites were included in analyses. Calls with a variant allele frequency (VAF)<5%, position coverage<30, or an allele frequency>=0.01 in ExAC were removed. To further improve the quality of indel calls, two additional filters were implemented: (1) Dustmasker (https://www.ncbi.nlm.nih.gov/IEB/ToolBox/CPP_DOC/lxr/source/src/app/dustmasker/) was used to identify low complexity genomic regions, and indels falling within these regions were discarded; (2) A pseudo-panel of normal samples was constructed, such that across the matched normal samples, all putative indel calls that failed Scalpel filters due to 'HighVafNormal' or 'HighAltCountNormal' were aggregated. All indels that failed in two or more samples from unique patients were filtered. These methods helped to eliminate remaining noisy calls which passed previous filtering steps.

[0112] Example variant calling workflow:

[0113] 1.
```
java -Djava.io.tmpdir=./temp -Xmx2g -jar mutect-1.1.7.jar -T MuTect -R hg19 --intervals chr1.intvl --input file:normal normal bam tumor bam --max_alt_alleles_in_normal_count 1000 --max_alt_alleles_in_normal_qscore_sum 37 --max_alt_allele_in_normal_fraction 0.05 --out tumor_normal/tumor_normal.chr1.out -vcf tumor_normal/tumor_normal.chr1.vcf --enable_extended_output --strand_artifact_power_threshold 0 -log tumor_normal.mutect.chr1.log 2>>‘tumor_normal.mutect.chr1.log;
```

[0114] 2.
```
metalfox.py -f1 tumor_normal/tumor_normal.chr1.out.keep -f3 tumor.bam -m wgEncodeCrgMapabilityAlign100mer.bedGraph.gz>tumor_normal.foxog_scored_added.out
```

[0115] 3.
```
scalpel-discovery --somatic --logs --numprocs 8 --tumor tumor bam --normal normal bam --bed capture_panel_v3.bed --ref hg19.fa 2>>tumor_normal.indels.log
```

[0116] 4.
```
java -jar snpEff.jar eff -t hg19 (tumor_normal.out.keep.sift.vcf/tumor_normal.somatic_indel.PASS.sift.vcf) -v>(tumor_normal.out.keep.eff.vcf/tumor_normal.somatic_indel.PASS.eff.vcf) 2>>tumor_normal.snpeff.log
```

[0117] Mutation Significance (MutSig) Analysis: VCFs were annotated and converted to a MAF format using Oncotator[20]. MAF files for all patients were merged and assessed for significant gene-centric mutation frequency using MutSigCV version 2 with default coverage and covariate tables provided by the Broad Institute[21]. Mutation Assessor[22] and ClinVar[23] were used to predict the functional impact of protein-coding mutations.

[0118] Copy Number Variation Analysis: Copy number calling was carried out using CNVKit v0.7.12.dev0[24]. All 59 matched-normal samples were used to calculate the pooled reference baseline using default parameters. Segmented log 2 ratios were used to call copy number gains and losses.

[0119] Identification of Prognostic Mutations: Multivariate Cox proportional hazard ratios were generated for each mutated gene feature as a binary factor across 59 liver metastasis-matched paired normal samples using the survival v2.40-1 R package. SNF subtype and Clinical Risk Score (CRS) were included as covariates in multivariate analyses. Ten-year overall survival was chosen as the primary endpoint of the analysis.

[0120] Microsatellite Instability (MSI) Analysis

[0121] H&E slides of normal and tumor specimens were reviewed by a molecular pathologist (Dr. Nora Joseph). Tumor sections with greater than 30% tumor percentage were used for DNA extraction by the Pinpoint Slide DNA Isolation System (Zymo Research). DNA was subsequently purified by using the Zymo-Spin I Column protocol. All samples were run on the Promega MSI 1.2 assay according to the FDA approved protocol and result interpretation. MSI testing was performed on 93 metastases with corresponding SNF subtypes of which 89 samples were successfully assayed. Four samples failed repeated testing.

[0122] Immunohistochemical Analysis

[0123] CRC liver metastases were preserved in formalin and embedded in paraffin. 5 μm tissue sections were created from paraffin blocks and mounted on glass slides. The slides were stained on Leica Bond RX Automatic Stainer using HTRC Bond Refine DAB protocol. After antigen retrieval treatment (epitope retrieval solution II, AR9640, Leica Biosystems) for 20 minutes, anti-human CD3 (DAKO, Cat#M7254, Clone: F7.2.38, mouse IgG) antibody (1:600) was applied on tissue sections for 25 minutes incubation. For CD8 staining, anti-human CD8 (DAKO, Cat#M7103, Clone: C8/144B, mouse IgG) antibody (1:400) was applied. The antigen-antibody binding was detected with Bond polymer refine detection (Leica Biosystems, DS9800). A coverslip was applied to the tissue sections. For Masson's trichrome staining, tissue sections were deparaffinized using heated Bouin's solution and then stained with Weigert's iron hematoxylin and Biebrich scarlet solutions. The tissue sections were then treated with phosphotungstic-phosphomolybdic acid and immediately stained with aniline blue solution. The tissue sections were rinsed and a coverslip was applied.

TABLE 2

Samples utilized for genome-wide analyses.

Sample ID	Institution	Source	microRNA	RNA Seq	Next Gen Seq
NS1	NorthShore Univ.	Liver Metastasis	x	x	x
NS10	NorthShore Univ.	Liver Metastasis	x	x	
NS11	NorthShore Univ.	Liver Metastasis	x	x	x
NS12	NorthShore Univ.	Liver Metastasis	x	x	x
NS13	NorthShore Univ.	Liver Metastasis	x	x	
NS14	NorthShore Univ.	Liver Metastasis	x	x	
NS15	NorthShore Univ.	Liver Metastasis	x	x	x
NS16	NorthShore Univ.	Liver Metastasis	x	x	
NS17	NorthShore Univ.	Liver Metastasis	x	x	
NS18	NorthShore Univ.	Liver Metastasis	x	x	x
NS19	NorthShore Univ.	Liver Metastasis	x	x	x
NS2	NorthShore Univ.	Liver Metastasis	x		
NS20	NorthShore Univ.	Liver Metastasis	x		x
NS21	NorthShore Univ.	Liver Metastasis	x	x	
NS22	NorthShore Univ.	Liver Metastasis	x		x
NS23	NorthShore Univ.	Liver Metastasis	x		x
NS24	NorthShore Univ.	Liver Metastasis	x	x	x
NS25	NorthShore Univ.	Liver Metastasis	x	x	x
NS26	NorthShore Univ.	Liver Metastasis	x		x
NS27	NorthShore Univ.	Liver Metastasis	x	x	
NS28	NorthShore Univ.	Liver Metastasis	x	x	
NS29	NorthShore Univ.	Liver Metastasis	x		x
NS3	NorthShore Univ.	Liver Metastasis	x	x	
NS30	NorthShore Univ.	Liver Metastasis	x	x	x
NS31	NorthShore Univ.	Liver Metastasis	x	x	x
NS32	NorthShore Univ.	Liver Metastasis	x	x	
NS33	NorthShore Univ.	Liver Metastasis	x		
NS34	NorthShore Univ.	Liver Metastasis	x	x	
NS35	NorthShore Univ.	Liver Metastasis	x	x	x
NS4	NorthShore Univ.	Liver Metastasis	x	x	x
NS5	NorthShore Univ.	Liver Metastasis	x	x	
NS6	NorthShore Univ.	Liver Metastasis	x	x	x
NS7	NorthShore Univ.	Liver Metastasis	x	x	x
NS8	NorthShore Univ.	Liver Metastasis	x	x	
NS9	NorthShore Univ.	Liver Metastasis	x	x	x
UC1	Univ. of Chicago	Liver Metastasis	x	x	
UC10	Univ. of Chicago	Liver Metastasis	x		
UC11	Univ. of Chicago	Liver Metastasis	x	x	x
UC12	Univ. of Chicago	Liver Metastasis	x		
UC13	Univ. of Chicago	Liver Metastasis	x		
UC14	Univ. of Chicago	Liver Metastasis	x	x	
UC15	Univ. of Chicago	Liver Metastasis	x	x	
UC16	Univ. of Chicago	Liver Metastasis	x		
UC17	Univ. of Chicago	Liver Metastasis	x	x	
UC18	Univ. of Chicago	Liver Metastasis	x	x	
UC19	Univ. of Chicago	Liver Metastasis	x	x	x
UC2	Univ. of Chicago	Liver Metastasis	x	x	

TABLE 2-continued

Samples utilized for genome-wide analyses.

Sample ID	Institution	Source	microRNA	RNA Seq	Next Gen Seq
UC20	Univ. of Chicago	Liver Metastasis	x	x	
UC21	Univ. of Chicago	Liver Metastasis	x	x	x
UC22	Univ. of Chicago	Liver Metastasis	x	x	
UC23	Univ. of Chicago	Liver Metastasis			x
UC24	Univ. of Chicago	Liver Metastasis	x	x	
UC25	Univ. of Chicago	Liver Metastasis	x	x	
UC26	Univ. of Chicago	Liver Metastasis	x		x
UC27	Univ. of Chicago	Liver Metastasis	x	x	x
UC28	Univ. of Chicago	Liver Metastasis	x	x	x
UC29	Univ. of Chicago	Liver Metastasis	x	x	x
UC3	Univ. of Chicago	Liver Metastasis	x		
UC30	Univ. of Chicago	Liver Metastasis	x	x	
UC31	Univ. of Chicago	Liver Metastasis	x	x	x
UC32	Univ. of Chicago	Liver Metastasis	x	x	
UC33	Univ. of Chicago	Liver Metastasis	x	x	x
UC34	Univ. of Chicago	Liver Metastasis	x	x	x
UC35	Univ. of Chicago	Liver Metastasis			x
UC36	Univ. of Chicago	Liver Metastasis	x		x
UC37	Univ. of Chicago	Liver Metastasis	x	x	x
UC38	Univ. of Chicago	Liver Metastasis	x		x
UC39	Univ. of Chicago	Liver Metastasis	x	x	
UC4	Univ. of Chicago	Liver Metastasis	x	x	
UC40	Univ. of Chicago	Liver Metastasis	x	x	
UC41	Univ. of Chicago	Liver Metastasis	x	x	x
UC42	Univ. of Chicago	Liver Metastasis	x	x	
UC43	Univ. of Chicago	Liver Metastasis	x	x	x
UC44	Univ. of Chicago	Liver Metastasis	x	x	
UC45	Univ. of Chicago	Liver Metastasis	x	x	x
UC46	Univ. of Chicago	Liver Metastasis	x	x	
UC47	Univ. of Chicago	Liver Metastasis	x	x	
UC48	Univ. of Chicago	Liver Metastasis	x		x
UC49	Univ. of Chicago	Liver Metastasis	x	x	x
UC5	Univ. of Chicago	Liver Metastasis	x	x	x
UC50	Univ. of Chicago	Liver Metastasis	x	x	
UC51	Univ. of Chicago	Liver Metastasis	x	x	x
UC52	Univ. of Chicago	Liver Metastasis	x	x	
UC53	Univ. of Chicago	Liver Metastasis	x	x	x
UC54	Univ. of Chicago	Liver Metastasis	x	x	
UC55	Univ. of Chicago	Liver Metastasis	x	x	x
UC56	Univ. of Chicago	Liver Metastasis		x	x
UC57	Univ. of Chicago	Liver Metastasis	x	x	x
UC58	Univ. of Chicago	Liver Metastasis	x	x	x
UC59	Univ. of Chicago	Liver Metastasis	x	x	x
UC6	Univ. of Chicago	Liver Metastasis		x	
UC60	Univ. of Chicago	Liver Metastasis			x
UC61	Univ. of Chicago	Liver Metastasis	x	x	
UC62	Univ. of Chicago	Liver Metastasis	x	x	x
UC63	Univ. of Chicago	Liver Metastasis	x		
UC64	Univ. of Chicago	Liver Metastasis	x		x
UC65	Univ. of Chicago	Liver Metastasis	x	x	
UC66	Univ. of Chicago	Liver Metastasis	x	x	
UC67	Univ. of Chicago	Liver Metastasis	x		
UC68	Univ. of Chicago	Liver Metastasis	x	x	x
UC69	Univ. of Chicago	Liver Metastasis	x		
UC7	Univ. of Chicago	Liver Metastasis	x	x	
UC70	Univ. of Chicago	Liver Metastasis	x	x	x
UC71	Univ. of Chicago	Liver Metastasis	x	x	
UC72	Univ. of Chicago	Liver Metastasis	x	x	
UC73	Univ. of Chicago	Liver Metastasis	x	x	x
UC74	Univ. of Chicago	Liver Metastasis	x	x	x
UC75	Univ. of Chicago	Liver Metastasis	x	x	
UC76	Univ. of Chicago	Liver Metastasis	x		x
UC77	Univ. of Chicago	Liver Metastasis	x		x
UC78	Univ. of Chicago	Liver Metastasis	x	x	x
UC79	Univ. of Chicago	Liver Metastasis	x	x	
UC8	Univ. of Chicago	Liver Metastasis	x	x	
UC80	Univ. of Chicago	Liver Metastasis	x	x	
UC81	Univ. of Chicago	Liver Metastasis	x	x	
UC82	Univ. of Chicago	Liver Metastasis	x	x	
UC83	Univ. of Chicago	Liver Metastasis	x	x	
UC84	Univ. of Chicago	Liver Metastasis	x	x	
UC85	Univ. of Chicago	Liver Metastasis	x	x	
UC86	Univ. of Chicago	Liver Metastasis	x		
UC9	Univ. of Chicago	Liver Metastasis	x	x	x

Tables 3A-C. Differentially expressed genes across SNF clusters in 93 metastatic RNA Sequencing samples identified by the limma-voom method. (A) Differentially expressed genes (DEGs) between SNF1 versus SNF2 and 3. (B) DEGs between SNF2 versus SNF1 and 3. (C) DEGs between SNF3 versus SNF1 and 2. Log 2FC: estimate of the log 2 fold-change corresponding to the contrast. Adj.P.Val: Benjamini-Hochberg corrected P-value. Cutoff values for DEGs are log 2FC=±1 and adj.P.Val≤0.05.

TABLE 3A

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000114113	RBP2	2.402377682	0.000208982
ENSG00000188176	SMTNL2	2.397349614	0.000243497
ENSG00000101958	GLRA2	1.849125462	0.014880259
ENSG00000165730	STOX1	1.814566368	0.000376488
ENSG00000124882	EREG	1.802200741	3.30361E−05
ENSG00000068615	REEP1	1.72856343	0.02439499
ENSG00000149295	DRD2	1.718068318	0.038733231
ENSG00000188883	KLRG2	1.686341802	0.015076777
ENSG00000184368	MAP7D2	1.670440677	0.042672544
ENSG00000130234	ACE2	1.558078536	0.011152632
ENSG00000164076	CAMKV	1.507861424	0.036206093
ENSG00000110195	FOLR1	1.452851117	0.049653874
ENSG00000168243	GNG4	1.442401071	0.002155582
ENSG00000135917	SLC19A3	1.420649708	5.72027E−05
ENSG00000186198	SLC51B	1.413076946	0.002412178
ENSG00000064195	DLX3	1.403694341	0.042259802
ENSG00000109321	AREG	1.374721044	1.5288E−05
ENSG00000151838	CCDC175	1.356610589	0.00125377
ENSG00000139292	LGR5	1.330918379	0.001109408
ENSG00000145569	FAM105A	1.275176254	9.64837E−08
ENSG00000134215	VAV3	1.269357856	3.00521E−05
ENSG00000155850	SLC26A2	1.261278624	0.008025503
ENSG00000102924	CBLN1	1.260630277	0.027551713
ENSG00000108576	SLC6A4	1.251556783	0.0342596
ENSG00000275004	ZNF280B	1.24127452	5.1556E−05
ENSG00000132821	VSTM2L	1.240352896	0.024453349
ENSG00000130055	GDPD2	1.212163873	0.016296313
ENSG00000144354	CDCA7	1.202383358	2.12792E−05
ENSG00000159409	CELF3	1.199684556	0.033506433
ENSG00000155380	SLC16A1	1.197394536	1.26489E−06
ENSG00000186564	FOXD2	1.194840276	0.001036938
ENSG00000181690	PLAG1	1.185059356	0.00538507
ENSG00000196604	POTEF	1.169865687	0.039795376
ENSG00000118557	PMFBP1	1.159904285	0.0152575
ENSG00000164649	CDCA7L	1.159525916	1.8842E−05
ENSG00000116299	KIAA1324	1.141930471	0.019276144
ENSG00000117834	SLC5A9	1.133319506	0.020497724
ENSG00000154639	CXADR	1.115878739	8.00911E−08
ENSG00000142606	MMEL1	1.113779984	0.019290196
ENSG00000021300	PLEKHB1	1.109828939	0.003560571
ENSG00000112742	TTK	1.107662416	1.46899E−05
ENSG00000158555	GDPD5	1.101681802	0.00095828
ENSG00000088325	TPX2	1.098363086	2.63438E−05
ENSG00000196172	ZNF681	1.098066536	0.001824751
ENSG00000254726	MEX3A	1.087467248	0.000197599
ENSG00000189431	RASSF10	1.086839686	0.008703152
ENSG00000164398	ACSL6	1.084221924	0.0152218
ENSG00000137251	TINAG	1.082801224	0.011697726
ENSG00000132970	WASF3	1.081994274	0.02734786

TABLE 3A-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000131747	TOP2A	1.078065148	8.1531E−05
ENSG00000000003	TSPAN6	1.066413046	2.51158E−06
ENSG00000188124	OR2AG2	1.065088681	0.012084353
ENSG00000198535	C2CD4A	1.062921578	0.016522229
ENSG00000166866	MYO1A	1.041611068	0.001184125
ENSG00000213160	KLHL23	1.039218214	2.88262E−07
ENSG00000161082	CELF5	1.033491448	0.041100425
ENSG00000164362	TERT	1.025951854	0.016841805
ENSG00000184933	OR6A2	1.02215216	0.008185591
ENSG00000104537	ANXA13	1.018421643	0.017649315
ENSG00000104147	OIP5	1.011329218	0.000574736
ENSG00000136425	CIB2	1.010255223	0.004913766
ENSG00000106541	AGR2	1.010190816	0.000511074
ENSG00000126003	PLAGL2	1.006386116	2.3823E−05
ENSG00000136982	DSCC1	1.004849438	0.000122738
ENSG00000117069	ST6GALNAC5	−1.000782426	0.007780424
ENSG00000102879	CORO1A	−1.001054276	0.000318174
ENSG00000214140	PRCD	−1.001428963	0.002533169
ENSG00000137868	STRA6	−1.001840186	0.02339985
ENSG00000113657	DPYSL3	−1.002137358	0.000167553
ENSG00000169902	TPST1	−1.002395305	8.10998E−05
ENSG00000127951	FGL2	−1.002497793	0.000642762
ENSG00000146859	TMEM140	−1.002747765	0.000108882
ENSG00000172243	CLEC7A	−1.003383024	0.000929502
ENSG00000144824	PHLDB2	−1.004769482	0.00011297
ENSG00000196209	SIRPB2	−1.005999695	6.78815E−05
ENSG00000204389	HSPA1A	−1.006401232	0.038503706
ENSG00000071282	LMCD1	−1.007393734	1.14568E−05
ENSG00000162461	SLC25A34	−1.007734946	0.000230625
ENSG00000168779	SHOX2	−1.008751338	0.029715421
ENSG00000213398	LCAT	−1.008987592	0.000376827
ENSG00000149591	TAGLN	−1.009349405	8.33812E−05
ENSG00000150656	CNDP1	−1.009526534	0.04648041
ENSG00000173918	C1QTNF1	−1.009692419	2.47492E−06
ENSG00000103544	C16orf62	−1.010080227	4.781E−05
ENSG00000164220	F2RL2	−1.010267071	0.004009132
ENSG00000005243	COPZ2	−1.010284615	3.00382E−05
ENSG00000150681	RGS18	−1.011124365	0.004238641
ENSG00000135046	ANXA1	−1.011681717	0.000329194
ENSG00000184588	PDE4B	−1.011804992	0.000489961
ENSG00000004399	PLXND1	−1.012137845	1.33346E−06
ENSG00000130270	ATP8B3	−1.0126323	0.001458946
ENSG00000155269	GPR78	−1.013738113	0.014942782
ENSG00000161835	GRASP	−1.014017589	0.000287209
ENSG00000078098	FAP	−1.015132052	7.35271E−05
ENSG00000007129	CEACAM21	−1.015538603	0.002250946
ENSG00000162849	KIF26B	−1.015776584	0.000624406
ENSG00000120913	PDLIM2	−1.016116229	1.07962E−07
ENSG00000129514	FOXA1	−1.017427806	0.020065896
ENSG00000169129	AFAP1L2	−1.017642893	0.000693535
ENSG00000133104	SPG20	−1.017758165	1.30418E−05
ENSG00000184979	USP18	−1.017784816	0.003386386
ENSG00000086288	NME8	−1.01848261	0.00069269
ENSG00000174837	EMR1	−1.018771074	0.028479292
ENSG00000170989	S1PR1	−1.019226184	0.000187363
ENSG00000185652	NTF3	−1.01939436	0.00782992
ENSG00000171700	RGS19	−1.021064945	1.02545E−05
ENSG00000166292	TMEM100	−1.021075304	0.009254341
ENSG00000135905	DOCK10	−1.022203289	0.00010271
ENSG00000145244	CORIN	−1.02236406	0.000378948
ENSG00000113389	NPR3	−1.022421244	0.000778194
ENSG00000183837	PNMA3	−1.022602374	0.028669553
ENSG00000142227	EMP3	−1.022753035	3.02792E−06
ENSG00000136689	IL1RN	−1.022894131	0.004970645
ENSG00000088538	DOCK3	−1.022986395	0.003476847
ENSG00000104267	CA2	−1.023079238	0.003597149
ENSG00000162946	DISC1	−1.023113136	3.83587E−05
ENSG00000182885	GPR97	−1.023512349	0.003836755
ENSG00000090339	ICAM1	−1.023933544	2.16095E−05
ENSG00000174004	NRROS	−1.025033931	0.001102818
ENSG00000134326	CMPK2	−1.025302594	0.000825354
ENSG00000178404	KIAA1731NL	−1.026263787	1.63415E−05
ENSG00000254535	PABPC4L	−1.026264785	0.000606648
ENSG00000127084	FGD3	−1.026564283	2.72501E−05
ENSG00000260729	RP11-106M3.2	−1.026686491	0.003808553
ENSG00000088756	ARHGAP28	−1.026798954	0.013969182
ENSG00000174640	SLCO2A1	−1.027077345	0.004601407
ENSG00000254521	SIGLEC12	−1.027098989	0.013153195
ENSG00000150995	ITPR1	−1.027862169	3.14471E−07
ENSG00000135094	SDS	−1.028193464	0.013303757
ENSG00000077092	RARB	−1.028239627	1.24729E−05
ENSG00000107518	ATRNL1	−1.028730709	0.002800469
ENSG00000135842	FAM129A	−1.028858655	6.49193E−06
ENSG00000134242	PTPN22	−1.02976135	0.00024393
ENSG00000135709	KIAA0513	−1.029785007	5.10681E−05
ENSG00000171033	PKIA	−1.029854887	0.047967857
ENSG00000141497	ZMYND15	−1.030036851	2.90319E−05
ENSG00000156113	KCNMA1	−1.031003391	0.002869868
ENSG00000004776	HSPB6	−1.031066746	0.002274733
ENSG00000143110	C1orf162	−1.0319018	4.781E−05
ENSG00000185634	SHC4	−1.031905167	0.002917639
ENSG00000132932	ATP8A2	−1.032621332	0.006321757
ENSG00000160469	BRSK1	−1.03284979	0.000460022
ENSG00000137094	DNAJB5	−1.033957151	6.18202E−06
ENSG00000129116	PALLD	−1.03409591	1.09763E−05
ENSG00000204682	CASC10	−1.034497917	0.00605214
ENSG00000197380	DACT3	−1.034720388	6.51406E−06
ENSG00000138185	ENTPD1	−1.034814376	1.26735E−05
ENSG00000164330	EBF1	−1.035602254	0.000146673
ENSG00000036530	CYP46A1	−1.035945787	0.008262352
ENSG00000151650	VENTX	−1.035991037	0.031368411
ENSG00000175262	C1orf127	−1.036174402	0.01204617
ENSG00000269404	SPIB	−1.036664975	0.013084021
ENSG00000144837	PLA1A	−1.037827634	0.01942901
ENSG00000171951	SCG2	−1.038502613	0.03101343
ENSG00000196923	PDLIM7	−1.03950379	2.10135E−05
ENSG00000178498	DTX3	−1.039873107	7.03238E−05
ENSG00000143387	CTSK	−1.040149202	1.05242E−05
ENSG00000160471	COX6B2	−1.040316079	0.002013588
ENSG00000157654	PALM2-AKAP2	−1.040535078	0.00119669
ENSG00000131015	ULBP2	−1.040894272	0.004465717
ENSG00000143995	MEIS1	−1.040926559	3.30344E−05
ENSG00000167549	CORO6	−1.041072554	0.004416835
ENSG00000137507	LRRC32	−1.041274101	1.5046E−05
ENSG00000167476	JSRP1	−1.042762963	0.00321037
ENSG00000162687	KCNT2	−1.043380463	0.000359668
ENSG00000167850	CD300C	−1.043537764	0.000492358
ENSG00000148516	ZEB1	−1.043553924	6.53044E−06
ENSG00000119699	TGFB3	−1.043677454	5.10681E−05
ENSG00000089692	LAG3	−1.043705335	0.000887602
ENSG00000101307	SIRPB1	−1.043945303	0.001335425
ENSG00000162426	SLC45A1	−1.043977512	0.000349024
ENSG00000124813	RUNX2	−1.044316033	5.63003E−05
ENSG00000166183	ASPG	−1.044697411	0.046582938
ENSG00000013619	MAMLD1	−1.04527249	3.14471E−07
ENSG00000139572	GPR84	−1.045520338	0.001236327
ENSG00000140519	RHCG	−1.045539492	0.038860595
ENSG00000049246	PER3	−1.045718783	5.42012E−05
ENSG00000160321	ZNF208	−1.04580772	0.01357857
ENSG00000140859	KIFC3	−1.045878857	5.19906E−05
ENSG00000138639	ARHGAP24	−1.045932518	4.62262E−05
ENSG00000266094	RASSF5	−1.04629921	4.08124E−05
ENSG00000169418	NPR1	−1.047205485	0.00235917
ENSG00000138944	KIAA1644	−1.047706437	0.001864123
ENSG00000139899	CBLN3	−1.047818775	5.96005E−05
ENSG00000067445	TRO	−1.04859493	1.16543E−05
ENSG00000169554	ZEB2	−1.049049731	1.27047E−05
ENSG00000161298	ZNF382	−1.050061162	2.08379E−05
ENSG00000057657	PRDM1	−1.050475131	2.76635E−05
ENSG00000186354	C9orf47	−1.050665373	0.007978122
ENSG00000105137	SYDE1	−1.050782007	2.58796E−06
ENSG00000121068	TBX2	−1.051370833	8.64705E−05
ENSG00000173320	STOX2	−1.052255578	0.002048736
ENSG00000128918	ALDH1A2	−1.052278199	0.002941967
ENSG00000196632	WNK3	−1.052391031	0.002434239
ENSG00000143552	NUP210L	−1.052581466	0.000741341
ENSG00000185100	ADSSL1	−1.052778945	6.589E−05
ENSG00000074966	TXK	−1.053158781	0.000514017
ENSG00000065413	ANKRD44	−1.053710376	1.313E−05
ENSG00000104951	IL4I1	−1.053776753	0.004869228

TABLE 3A-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000107738	C10orf54	−1.053866868	6.78455E−07
ENSG00000082014	SMARCD3	−1.054298277	6.10459E−06
ENSG00000244242	IFITM10	−1.05435803	3.12165E−05
ENSG00000129244	ATP1B2	−1.054434713	0.000491418
ENSG00000176049	JAKMIP2	−1.054842449	0.016921277
ENSG00000112799	LY86	−1.055140672	0.006357425
ENSG00000153064	BANK1	−1.055342773	0.021723394
ENSG00000172322	CLEC12A	−1.05774634	0.005306616
ENSG00000074660	SCARF1	−1.05809983	2.82629E−07
ENSG00000146054	TRIM7	−1.058384682	0.017215382
ENSG00000171533	MAP6	−1.058716842	2.04347E−05
ENSG00000187800	PEAR1	−1.05904284	3.9877E−05
ENSG00000154734	ADAMTS1	−1.059294153	0.000810995
ENSG00000113721	PDGFRB	−1.059329869	4.81498E−05
ENSG00000186469	GNG2	−1.059346757	3.46938E−05
ENSG00000095370	SH2D3C	−1.059764088	3.2622E−06
ENSG00000185338	SOCS1	−1.060525597	0.000457649
ENSG00000145284	SCD5	−1.060596058	0.000322701
ENSG00000108691	CCL2	−1.0613407	0.000759205
ENSG00000049249	TNFRSF9	−1.061690428	0.000508862
ENSG00000118849	RARRES1	−1.062423869	0.000530439
ENSG00000258405	ZNF578	−1.062551598	0.007548984
ENSG00000010810	FYN	−1.063074191	0.000265018
ENSG00000166825	ANPEP	−1.063700087	0.005121934
ENSG00000204131	NHSL2	−1.063791035	0.000195959
ENSG00000105472	CLEC11A	−1.064427076	1.97624E−06
ENSG00000148175	STOM	−1.065098031	1.58442E−05
ENSG00000118514	ALDH8A1	−1.065635125	0.036640022
ENSG00000109944	C11orf63	−1.065705697	0.000368205
ENSG00000205413	SAMD9	−1.066198494	7.82876E−05
ENSG00000204642	HLA-F	−1.066694092	0.001024249
ENSG00000123342	MMP19	−1.066860848	0.002186035
ENSG00000136383	ALPK3	−1.067183406	0.001228773
ENSG00000132031	MATN3	−1.067240512	0.019227324
ENSG00000186074	CD300LF	−1.06734085	0.000615876
ENSG00000105711	SCN1B	−1.067554069	4.81558E−05
ENSG00000178726	THBD	−1.068320198	0.000108526
ENSG00000153956	CACNA2D1	−1.068480709	8.11946E−06
ENSG00000137573	SULF1	−1.069334753	0.001017246
ENSG00000106605	BLVRA	−1.069357577	0.000137105
ENSG00000169085	C8orf46	−1.069479551	0.033990634
ENSG00000132357	CARD6	−1.069897645	1.22507E−05
ENSG00000150337	FCGR1A	−1.070347526	0.005282353
ENSG00000071967	CYBRD1	−1.070482987	0.000373622
ENSG00000188921	PTPLAD2	−1.070615287	6.60266E−05
ENSG00000178860	MSC	−1.07066421	6.65599E−06
ENSG00000145107	TM4SF19	−1.071086564	0.002429768
ENSG00000121207	LRAT	−1.071196068	0.007850145
ENSG00000143819	EPHX1	−1.071596274	0.000873153
ENSG00000165646	SLC18A2	−1.071809927	0.010164474
ENSG00000131471	AOC3	−1.072052773	7.17896E−06
ENSG00000035862	TIMP2	−1.072069427	1.48428E−05
ENSG00000125510	OPRL1	−1.072672553	0.00056955
ENSG00000080493	SLC4A4	−1.072857311	0.006470904
ENSG00000113580	NR3C1	−1.073346897	1.05502E−05
ENSG00000184613	NELL2	−1.074137359	0.010006497
ENSG00000183186	C2CD4C	−1.074179971	0.002277851
ENSG00000206052	DOK6	−1.074258727	0.001001334
ENSG00000137691	C11orf70	−1.074374696	0.002354684
ENSG00000197816	CCDC180	−1.075377114	0.000562678
ENSG00000123610	TNFAIP6	−1.075504166	0.001487586
ENSG00000145431	PDGFC	−1.07565821	2.33046E−05
ENSG00000077420	APBB1IP	−1.075833206	0.000148168
ENSG00000011600	TYROBP	−1.07691373	0.000149906
ENSG00000136167	LCP1	−1.077069203	0.000284648
ENSG00000166780	C16orf45	−1.078697479	1.14032E−06
ENSG00000164440	TXLNB	−1.078844273	0.00150505
ENSG00000099864	PALM	−1.079055262	7.4755E−05
ENSG00000108798	ABI3	−1.079131192	1.00502E−05
ENSG00000134571	MYBPC3	−1.079153579	0.00384447
ENSG00000188171	ZNF626	−1.079313846	0.00050143
ENSG00000121361	KCNJ8	−1.079416303	0.000658717
ENSG00000155761	SPAG17	−1.079523013	0.019849521
ENSG00000134460	IL2RA	−1.07982295	0.00017803
ENSG00000069667	RORA	−1.080113903	0.000230625

TABLE 3A-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000143119	CD53	−1.080681878	8.413E−05
ENSG00000166963	MAP1A	−1.08130821	2.38468E−06
ENSG00000185386	MAPK11	−1.08154262	6.53044E−06
ENSG00000073150	PANX2	−1.082028358	0.010100591
ENSG00000153093	ACOXL	−1.082303955	0.027831493
ENSG00000027075	PRKCH	−1.082894115	1.26489E−06
ENSG00000149781	FERMT3	−1.083400399	1.39654E−06
ENSG00000164088	PPM1M	−1.083568678	4.71788E−07
ENSG00000106689	LHX2	−1.083713658	0.005294238
ENSG00000115956	PLEK	−1.083751872	7.99128E−05
ENSG00000101017	CD40	−1.085183047	0.000439681
ENSG00000162722	TRIM58	−1.085234165	0.036793838
ENSG00000128274	A4GALT	−1.085847949	0.000424965
ENSG00000101265	RASSF2	−1.086241441	4.54694E−06
ENSG00000133800	LYVE1	−1.087559122	0.034749779
ENSG00000162367	TAL1	−1.087642472	0.000404758
ENSG00000127220	ABHD8	−1.088170824	0.000447151
ENSG00000090376	IRAK3	−1.088340885	1.56288E−05
ENSG00000081818	PCDHB4	−1.088478389	0.025502916
ENSG00000117586	TNFSF4	−1.089585956	1.64751E−05
ENSG00000115165	CYTIP	−1.09091077	6.22813E−05
ENSG00000137959	IFI44L	−1.091015582	0.020972087
ENSG00000117228	GBP1	−1.09132325	0.000309421
ENSG00000172403	SYNPO2	−1.091326944	4.11799E−05
ENSG00000020181	GPR124	−1.091663914	3.29587E−06
ENSG00000151702	FLI1	−1.091781691	6.18202E−06
ENSG00000139625	MAP3K12	−1.093430672	1.91479E−07
ENSG00000164236	ANKRD33B	−1.094590362	8.73266E−07
ENSG00000186340	THBS2	−1.095496627	0.000173743
ENSG00000271605	MILR1	−1.096240331	0.000158482
ENSG00000115232	ITGA4	−1.09626015	3.16481E−05
ENSG00000127129	EDN2	−1.096508376	0.019148295
ENSG00000182013	PNMAL1	−1.096652021	0.003136705
ENSG00000204262	COL5A2	−1.097604394	4.0212E−05
ENSG00000131435	PDLIM4	−1.099355604	0.007330896
ENSG00000183580	FBXL7	−1.09952859	1.11007E−05
ENSG00000133401	PDZD2	−1.100262075	0.000872012
ENSG00000171236	LRG1	−1.101288852	0.024666056
ENSG00000140678	ITGAX	−1.102029983	0.000175407
ENSG00000165617	DACT1	−1.102233742	2.29257E−05
ENSG00000132965	ALOX5AP	−1.10283166	0.000205549
ENSG00000232629	HLA-DQB2	−1.102911936	0.003997252
ENSG00000162733	DDR2	−1.103417294	7.23692E−06
ENSG00000169122	FAM110B	−1.103515248	0.00012276
ENSG00000155307	SAMSN1	−1.103960983	0.000360639
ENSG00000185483	ROR1	−1.104126239	0.000103448
ENSG00000053328	METTL24	−1.105532104	0.000503779
ENSG00000182263	FIGN	−1.106760156	0.001174942
ENSG00000142694	EVA1B	−1.106774972	1.3873E−05
ENSG00000184986	TMEM121	−1.107016608	0.002028343
ENSG00000182866	LCK	−1.108219651	0.00105822
ENSG00000156006	NAT2	−1.108306929	4.32466E−05
ENSG00000171817	ZNF540	−1.108424962	0.000668849
ENSG00000138615	CILP	−1.108544385	0.00140159
ENSG00000095321	CRAT	−1.108933986	6.099E−06
ENSG00000131018	SYNE1	−1.109202846	2.47631E−05
ENSG00000178573	MAF	−1.109395092	2.93627E−06
ENSG00000087589	CASS4	−1.109552356	5.12081E−06
ENSG00000133256	PDE6B	−1.109657156	0.003190935
ENSG00000138829	FBN2	−1.110204802	0.018183516
ENSG00000173641	HSPB7	−1.110988949	0.000929502
ENSG00000124496	TRERF1	−1.111200775	6.18202E−06
ENSG00000150637	CD226	−1.111232082	0.000394449
ENSG00000139737	SLAIN1	−1.112090463	0.006838191
ENSG00000164692	COL1A2	−1.112403098	5.56759E−05
ENSG00000135480	KRT7	−1.112877225	4.80699E−05
ENSG00000117091	CD48	−1.113270186	0.000261918
ENSG00000177294	FBXO39	−1.113293341	0.00072053
ENSG00000149380	P4HA3	−1.114113044	1.67292E−05
ENSG00000130487	KLHDC7B	−1.114285337	0.000474403
ENSG00000172348	RCAN2	−1.115210077	0.000246565
ENSG00000120129	DUSP1	−1.115785394	0.000400056
ENSG00000117016	RIMS3	−1.116823963	7.45298E−05
ENSG00000177409	SAMD9L	−1.117434192	0.000700465
ENSG00000140030	GPR65	−1.118044245	9.40358E−06

TABLE 3A-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000163239	TDRD10	−1.118422854	0.000907887
ENSG00000198879	SFMBT2	−1.118938964	1.06695E−05
ENSG00000147408	CSGALNACT1	−1.119739001	0.000192521
ENSG00000182809	CRIP2	−1.120605935	2.38468E−06
ENSG00000175003	SLC22A1	−1.121177319	0.031107642
ENSG00000133985	TTC9	−1.121442899	9.18726E−05
ENSG00000176438	SYNE3	−1.121646511	1.01098E−06
ENSG00000092096	SLC22A17	−1.121778181	1.87861E−05
ENSG00000137726	FXYD6	−1.122399792	0.000104671
ENSG00000171051	FPR1	−1.122549291	0.000335715
ENSG00000174945	AMZ1	−1.124101157	3.39034E−05
ENSG00000146112	PPP1R18	−1.124331805	1.58453E−07
ENSG00000184113	CLDN5	−1.1251397	0.000995088
ENSG00000049768	FOXP3	−1.125765608	0.00019175
ENSG00000134955	SLC37A2	−1.125880339	4.38625E−06
ENSG00000164604	GPR85	−1.126590857	0.004144476
ENSG00000135925	WNT10A	−1.126950717	0.017351572
ENSG00000181804	SLC9A9	−1.12790158	0.001278941
ENSG00000265107	GJA5	−1.128189705	0.000131847
ENSG00000225614	ZNF469	−1.128348931	1.58442E−05
ENSG00000235568	NFAM1	−1.128563754	1.33212E−06
ENSG00000138172	CALHM2	−1.12879888	6.63213E−07
ENSG00000087116	ADAMTS2	−1.129190361	3.2622E−06
ENSG00000093072	CECR1	−1.129217403	0.000164657
ENSG00000182327	GLTPD2	−1.129995159	0.035168166
ENSG00000160219	GAB3	−1.131016525	2.62136E−06
ENSG00000130635	COL5A1	−1.131597309	3.29885E−06
ENSG00000149633	KIAA1755	−1.131780689	4.09908E−06
ENSG00000184058	TBX1	−1.131814913	0.00034455
ENSG00000163219	ARHGAP25	−1.132316175	1.80964E−06
ENSG00000084110	HAL	−1.132621911	0.049765672
ENSG00000203883	SOX18	−1.132872117	4.38273E−06
ENSG00000139278	GLIPR1	−1.133166488	1.09064E−05
ENSG00000168077	SCARA3	−1.133251266	0.00666479
ENSG00000173535	TNFRSF10C	−1.133514942	0.000447151
ENSG00000043462	LCP2	−1.133719047	1.68559E−05
ENSG00000240771	ARHGEF25	−1.134623068	1.98003E−06
ENSG00000159674	SPON2	−1.135017344	3.86458E−07
ENSG00000184349	EFNA5	−1.135927178	0.000210271
ENSG00000145623	OSMR	−1.13622243	1.44968E−05
ENSG00000005249	PRKAR2B	−1.136701435	0.000624934
ENSG00000198417	MT1F	−1.137534728	0.000779952
ENSG00000125740	FOSB	−1.138518114	0.01115871
ENSG00000169604	ANTXR1	−1.138929461	0.000518846
ENSG00000008513	ST3GAL1	−1.139346894	1.3891E−05
ENSG00000153162	BMP6	−1.140070502	0.001057195
ENSG00000117525	F3	−1.140080597	5.63035E−05
ENSG00000024422	EHD2	−1.140832352	3.86458E−07
ENSG00000101955	SRPX	−1.140968253	0.00181741
ENSG00000126759	CFP	−1.141115715	0.000103448
ENSG00000174130	TLR6	−1.141472276	1.61997E−05
ENSG00000140937	CDH11	−1.141735103	4.91461E−05
ENSG00000144229	THSD7B	−1.141903892	0.005178232
ENSG00000165633	VSTM4	−1.142100677	1.40047E−06
ENSG00000160883	HK3	−1.142242025	0.000156299
ENSG00000106366	SERPINE1	−1.142993544	0.00219023
ENSG00000124491	F13A1	−1.144331261	0.003481187
ENSG00000135363	LMO2	−1.145868483	0.000110163
ENSG00000157017	GHRL	−1.146256277	0.00045037
ENSG00000185862	EVI2B	−1.146362154	0.00015935
ENSG00000188783	PRELP	−1.146456575	0.000530734
ENSG00000154721	JAM2	−1.146492986	5.99703E−05
ENSG00000107186	MPDZ	−1.14667538	1.80809E−05
ENSG00000141968	VAV1	−1.147075794	4.49639E−05
ENSG00000225968	ELFN1	−1.147216786	0.000330204
ENSG00000147697	GSDMC	−1.147240602	0.002444374
ENSG00000175264	CHST1	−1.147664007	2.42428E−06
ENSG00000214456	PLIN5	−1.147759689	0.034248162
ENSG00000186827	TNFRSF4	−1.148544774	6.02213E−05
ENSG00000136286	MYO1G	−1.148977907	1.26977E−06
ENSG00000163563	MNDA	−1.149208708	3.43305E−05
ENSG00000150471	LPHN3	−1.149573788	4.94402E−05
ENSG00000136842	TMOD1	−1.150027249	0.012434916
ENSG00000170962	PDGFD	−1.15005092	0.004180529
ENSG00000188596	CFAP54	−1.150400084	0.000191136

TABLE 3A-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000169136	ATF5	−1.151263756	0.000496023
ENSG00000172716	SLFN11	−1.151731402	2.06385E−06
ENSG00000171049	FPR2	−1.151774052	0.009388316
ENSG00000134321	RSAD2	−1.15268933	0.001401716
ENSG00000115252	PDE1A	−1.152693629	4.38625E−06
ENSG00000169248	CXCL11	−1.152849475	0.038859034
ENSG00000166927	MS4A7	−1.153085729	0.000208366
ENSG00000158186	MRAS	−1.153571411	1.93937E−06
ENSG00000167680	SEMA6B	−1.154940426	1.13595E−06
ENSG00000010310	GIPR	−1.155433522	1.33594E−05
ENSG00000106123	EPHB6	−1.156630456	0.003812667
ENSG00000170786	SDR16C5	−1.157339434	0.02161042
ENSG00000118473	SGIP1	−1.158832566	6.66812E−06
ENSG00000166432	ZMAT1	−1.159213368	3.16481E−05
ENSG00000176014	TUBB6	−1.159261511	6.51487E−07
ENSG00000177374	HIC1	−1.159337792	4.89951E−07
ENSG00000143502	SUSD4	−1.159827297	0.009295065
ENSG00000120337	TNFSF18	−1.160871924	0.000855507
ENSG00000119138	KLF9	−1.162445981	3.66474E−05
ENSG00000124334	IL9R	−1.162572201	0.002278566
ENSG00000147573	TRIM55	−1.162600898	0.041543957
ENSG00000186994	KANK3	−1.16339897	2.20908E−05
ENSG00000109113	RAB34	−1.164082237	2.07859E−06
ENSG00000182168	UNC5C	−1.16408554	3.10231E−06
ENSG00000196569	LAMA2	−1.164637929	0.000695574
ENSG00000131831	RAI2	−1.164930933	0.000153154
ENSG00000110446	SLC15A3	−1.165008055	9.45503E−06
ENSG00000166923	GREMI	−1.165067579	0.008425316
ENSG00000119865	CNRIP1	−1.1653631	2.93382E−06
ENSG00000204442	FAM155A	−1.165398098	0.039253389
ENSG00000122986	HVCN1	−1.165640049	4.05188E−05
ENSG00000167895	TMC8	−1.166270436	0.000274175
ENSG00000189056	RELN	−1.1663162	0.008258713
ENSG00000255587	RAB44	−1.166543722	0.000531022
ENSG00000125538	IL1B	−1.166866232	0.002501545
ENSG00000115590	IL1R2	−1.166984229	0.000426636
ENSG00000135063	FAM189A2	−1.167428531	0.007331374
ENSG00000107099	DOCK8	−1.167694574	4.61847E−06
ENSG00000137841	PLCB2	−1.168442317	1.94372E−05
ENSG00000232810	TNF	−1.16848809	0.001389679
ENSG00000242574	HLA-DMB	−1.168729004	3.57708E−05
ENSG00000130052	STARD8	−1.168935307	1.7421E−05
ENSG00000122641	INHBA	−1.169397155	0.000183548
ENSG00000181007	ZFP82	−1.169814254	0.000464191
ENSG00000169026	MFSD7	−1.170266056	1.20046E−05
ENSG00000078596	ITM2A	−1.170384262	0.00189795
ENSG00000165521	EML5	−1.170468916	0.001052901
ENSG00000163359	COL6A3	−1.170669016	2.95551E−05
ENSG00000167077	MEI1	−1.171680933	7.46667E−06
ENSG00000160791	CCR5	−1.171845258	3.16236E−05
ENSG00000173698	GPR64	−1.172686597	0.043142038
ENSG00000115935	WIPF1	−1.173078636	8.06061E−06
ENSG00000182853	VMO1	−1.173308348	0.004895509
ENSG00000150048	CLEC1A	-1.174214173	1.31665E−05
ENSG00000106823	ECM2	−1.174646561	9.44593E−06
ENSG00000146122	DAAM2	−1.174740771	6.25084E−06
ENSG00000105366	SIGLEC8	−1.176430354	0.007019332
ENSG00000185499	MUC1	−1.176632863	0.027474941
ENSG00000159189	C1QC	−1.176676781	8.78221E−05
ENSG00000171488	LRRC8C	−1.177362834	4.73932E−07
ENSG00000182175	RGMA	−1.177716915	5.42012E−05
ENSG00000182871	COL18A1	−1.178386322	1.58362E−05
ENSG00000135898	GPR55	−1.1786331	0.04168832
ENSG00000127472	PLA2G5	−1.179871732	0.001987752
ENSG00000244607	CCDC13	-1.179985727	0.00065737
ENSG00000164197	RNF180	-1.180272508	6.62915E−06
ENSG00000179909	ZNF154	−1.180353169	6.86309E−07
ENSG00000173546	CSPG4	−1.18060396	0.000105814
ENSG00000154822	PLCL2	−1.180646062	4.8614E−06
ENSG00000130775	THEMIS2	−1.181185522	5.4965E−06
ENSG00000134532	SOX5	−1.181650351	0.000533483
ENSG00000100336	APOL4	−1.182157909	0.000220807
ENSG00000084636	COL16A1	−1.183034006	1.08776E−05
ENSG00000010327	STAB1	−1.183814881	4.6063E−06
ENSG00000139187	KLRG1	−1.18393578	0.000242333

TABLE 3A-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000164741	DLC1	–1.184152784	1.34948E–06
ENSG00000231672	DIRC3	–1.185149757	0.000243148
ENSG00000065325	GLP2R	–1.185304374	0.00219023
ENSG00000198223	CSF2RA	–1.185323954	8.52127E–06
ENSG00000140511	HAPLN3	–1.185925451	2.10135E–05
ENSG00000198756	COLGALT2	–1.186158932	0.005416943
ENSG00000005381	MPO	–1.186385139	0.005928183
ENSG00000154319	FAM167A	–1.186397209	0.000388261
ENSG00000178297	TMPRSS9	–1.186723965	0.01349752
ENSG00000104447	TRPS1	–1.187451768	2.52627E–06
ENSG00000166035	LIPC	–1.187870772	0.029387324
ENSG00000189350	FAM179A	–1.18806183	3.32172E–05
ENSG00000115380	EFEMP1	–1.188320205	6.88103E–05
ENSG00000167613	LAIR1	–1.188563461	7.82772E–06
ENSG00000139970	RTN1	–1.189584441	1.07408E–06
ENSG00000182050	MGAT4C	–1.189786392	0.017909786
ENSG00000123338	NCKAP1L	–1.18998499	4.27658E–06
ENSG00000075340	ADD2	–1.190068477	0.009190393
ENSG00000000938	FGR	–1.190229233	1.94053E–05
ENSG00000180871	CXCR2	–1.191139331	0.000491418
ENSG00000174600	CMKLR1	–1.191782971	8.38988E–05
ENSG00000099260	PALMD	–1.191848962	0.000119091
ENSG00000221866	PLXNA4	–1.192245818	6.84456E–05
ENSG00000142748	FCN3	–1.192261941	0.042493263
ENSG00000132530	XAF1	–1.19264312	0.00024758
ENSG00000108821	COL1A1	–1.192686522	2.06351E–05
ENSG00000158163	DZIP1L	–1.192924992	9.62415E–07
ENSG00000173917	HOXB2	–1.195630744	1.35023E–06
ENSG00000198300	PEG3	–1.196089492	6.73493E–05
ENSG00000137857	DUOX1	–1.196165246	0.006588702
ENSG00000118596	SLC16A7	–1.196287822	3.89164E–05
ENSG00000005513	SOX8	–1.196891539	0.023936211
ENSG00000111962	UST	–1.197117891	0.001217187
ENSG00000109738	GLRB	–1.197213302	0.002769453
ENSG00000175287	PHYHD1	–1.199148936	0.000601286
ENSG00000133574	GIMAP4	–1.199331097	0.000108277
ENSG00000118523	CTGF	–1.199512142	5.89074E–05
ENSG00000101298	SNPH	–1.199878151	2.06707E–06
ENSG00000137558	PI15	–1.200980713	0.001198322
ENSG00000162654	GBP4	–1.201334905	0.000644827
ENSG00000159761	C1orf86	–1.201521832	0.00031607
ENSG00000105383	CD33	–1.201802317	6.589E–05
ENSG00000067798	NAV3	–1.201989516	0.000172006
ENSG00000129675	ARHGEF6	–1.202118353	1.77842E–06
ENSG00000173258	ZNF483	–1.202983572	0.005882316
ENSG00000244694	PTCHD4	–1.204273641	0.012782289
ENSG00000100321	SYNGR1	–1.204841818	0.000255014
ENSG00000171115	GIMAP8	–1.204860222	3.88115E–05
ENSG00000003989	SLC7A2	–1.204966223	0.006561721
ENSG00000198108	CHSY3	–1.20499247	2.43913E–06
ENSG00000131187	F12	–1.205066496	0.01116517
ENSG00000172260	NEGR1	–1.205715615	0.004931555
ENSG00000241644	INMT	–1.20587723	0.000143646
ENSG00000177103	DSCAML1	–1.206484225	0.007907869
ENSG00000250120	PCDHA10	-1.206740837	0.045672655
ENSG00000110076	NRXN2	–1.207544301	6.05614E–05
ENSG00000184557	SOCS3	–1.208085693	9.71093E–05
ENSG00000099860	GADD45B	–1.208300182	0.000141517
ENSG00000120875	DUSP4	–1.208891098	0.000179051
ENSG00000188064	WNT7B	–1.209142013	0.010610886
ENSG00000134516	DOCK2	–1.209168062	1.49442E–05
ENSG00000072952	MRVI1	–1.209447861	4.7121E–06
ENSG00000181291	TMEM132E	–1.209659251	0.00218064
ENSG00000165124	SVEP1	–1.20983018	3.0356E–05
ENSG00000155970	MICU3	–1.209865134	8.55803E–06
ENSG00000146374	RSPO3	–1.209873799	0.001275565
ENSG00000111728	ST8SIA1	–1.21101385	0.004710055
ENSG00000120833	SOCS2	–1.211505742	1.64174E–05
ENSG00000178175	ZNF366	–1.211564579	2.31768E–05
ENSG00000185737	NRG3	–1.212342654	0.001327903
ENSG00000152527	PLEKHH2	–1.213090507	5.57419E–05
ENSG00000134874	DZIP1	–1.21356678	7.57031E–08
ENSG00000144642	RBMS3	–1.213652734	3.86952E–06
ENSG00000170956	CEACAM3	–1.21382941	0.004531583
ENSG00000113749	HRH2	–1.213893715	0.00057991

TABLE 3A-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000062524	LTK	–1.213934508	0.007342167
ENSG00000130755	GMFG	–1.214020953	4.1255E–06
ENSG00000109956	B3GAT1	–1.214052199	0.008399257
ENSG00000122254	HS3ST2	–1.215727907	0.006137718
ENSG00000136999	NOV	–1.216119385	2.26194E–05
ENSG00000008118	CAMK1G	–1.216465351	0.000323103
ENSG00000077782	FGFR1	–1.216659536	7.61758E–05
ENSG00000105329	TGFB1	–1.216730912	7.548E–07
ENSG00000125430	HS3ST3B1	–1.217189858	0.000204523
ENSG00000184271	POU6F1	–1.217315751	3.16218E–07
ENSG00000107611	CUBN	–1.217602366	9.03133E–06
ENSG00000103313	MEFV	–1.217686693	0.000901215
ENSG00000104368	PLAT	–1.219462117	1.60205E–05
ENSG00000187037	GPR141	–1.219708612	0.00034455
ENSG00000224389	C4B	–1.219744569	0.03778999
ENSG00000204252	HLA-DOA	–1.219840235	2.9222E–05
ENSG00000168309	FAM107A	–1.220022435	0.00054014
ENSG00000100344	PNPLA3	–1.220399677	0.044051237
ENSG00000130558	OLFM1	–1.220810425	0.004399836
ENSG00000198046	ZNF667	–1.220830046	5.28912E–06
ENSG00000108823	SGCA	–1.221078587	0.000298154
ENSG00000158517	NCF1	–1.221294717	0.000831881
ENSG00000239998	LILRA2	–1.22159887	3.7788E–05
ENSG00000123095	BHLHE41	–1.222564294	5.59088E–06
ENSG00000152049	KCNE4	–1.222624045	4.08965E–06
ENSG00000135272	MDFIC	–1.223105728	2.00784E–06
ENSG00000143369	ECM1	–1.223201413	1.56575E–05
ENSG00000010610	CD4	–1.223221024	1.22209E–06
ENSG00000141622	RNF165	–1.223643902	0.008455567
ENSG00000102383	ZDHHC15	–1.224320897	0.006470904
ENSG00000163565	IFI16	–1.224602115	4.92172E–06
ENSG00000186818	LILRB4	–1.22555358	1.80011E–05
ENSG00000157765	SLC34A2	–1.22590591	0.012532003
ENSG00000118004	COLEC11	–1.226439558	0.001119969
ENSG00000077264	PAK3	–1.226648361	0.004295558
ENSG00000139926	FRMD6	–1.226682397	8.31715E–07
ENSG00000198796	ALPK2	–1.227302741	0.000130756
ENSG00000173210	ABLIM3	–1.227546546	0.001906516
ENSG00000158246	FAM46B	–1.227774062	0.001327891
ENSG00000135835	KIAA1614	–1.227859531	1.09105E–05
ENSG00000120658	ENOX1	–1.22871094	0.000120292
ENSG00000145362	ANK2	–1.229270391	0.000539649
ENSG00000157514	TSC22D3	–1.22944806	2.10135E–05
ENSG00000129038	LOXL1	–1.229597535	9.30958E–08
ENSG00000010295	IFFO1	–1.230998441	1.04551E–07
ENSG00000196218	RYR1	–1.231926697	0.001466195
ENSG00000169495	HTRA4	–1.232533396	0.000269144
ENSG00000183098	GPC6	–1.23264938	3.44828E–06
ENSG00000019102	VSIG2	–1.232939228	0.00487217
ENSG00000172578	KLHL6	–1.23385044	5.71004E–05
ENSG00000173421	CCDC36	–1.233872763	5.08468E–06
ENSG00000185215	TNFAIP2	–1.233905637	1.92084E–05
ENSG00000237541	HLA-DQA2	–1.234364566	0.017383524
ENSG00000067840	PDZD4	–1.234984539	8.09621E–05
ENSG00000175879	HOXD8	–1.235002643	0.047873132
ENSG00000156299	TIAM1	–1.235032713	2.84269E–06
ENSG00000175489	LRRC25	–1.23504695	1.50406E–05
ENSG00000125551	PLGLB2	–1.235824933	0.020069572
ENSG00000187116	LILRA5	–1.236606775	0.001666785
ENSG00000162711	NLRP3	–1.237364079	2.18735E–06
ENSG00000081237	PTPRC	–1.237467457	2.97105E–05
ENSG00000008516	MMP25	–1.237731453	1.0864E–05
ENSG00000079215	SLC1A3	–1.23840385	0.000415863
ENSG00000108387	SEPT4	–1.238949239	6.53044E–06
ENSG00000179954	SSC5D	–1.239358618	5.02948E–06
ENSG00000161929	SCIMP	–1.240027423	0.00011331
ENSG00000115556	PLCD4	–1.240338243	0.000411355
ENSG00000204287	HLA-DRA	–1.240436516	0.000138259
ENSG00000239697	TNFSF12	–1.24050702	5.97701E–08
ENSG00000182492	BGN	–1.240775055	1.62675E–05
ENSG00000166106	ADAMTS15	–1.240999726	0.010601951
ENSG00000100342	APOL1	–1.241062252	6.18162E–05
ENSG00000111077	TNS2	–1.241479647	2.21115E–07
ENSG00000104899	AMH	–1.241538324	0.001198322
ENSG00000173372	C1QA	–1.241766344	0.000504732

TABLE 3A-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000204381	LAYN	−1.242542509	5.05882E−06
ENSG00000163600	ICOS	−1.242894599	0.001098585
ENSG00000169282	KCNAB1	−1.243743285	0.001110994
ENSG00000167693	NXN	−1.243837222	6.1219E−06
ENSG00000133063	CHIT1	−1.243932804	0.016066024
ENSG00000069431	ABCC9	−1.244417217	2.20898E−05
ENSG00000163145	C1QTNF7	−1.245214393	0.000835544
ENSG00000136859	ANGPTL2	−1.245224033	4.92172E−06
ENSG00000189129	PLAC9	−1.24534814	0.000221819
ENSG00000114654	EFCC1	−1.245378439	5.40913E−05
ENSG00000166405	RIC3	−1.245781251	0.004240274
ENSG00000117154	IGSF21	−1.245898827	0.003965059
ENSG00000184828	ZBTB7C	−1.246309911	0.000607743
ENSG00000115461	IGFBP5	−1.246924626	0.000204529
ENSG00000019582	CD74	−1.247020794	3.22201E−05
ENSG00000162520	SYNC	−1.247398028	8.37346E−06
ENSG00000140090	SLC24A4	−1.247409502	1.63415E−05
ENSG00000120949	TNFRSF8	−1.247938845	0.000415863
ENSG00000196126	HLA-DRB1	−1.248165776	5.49421E−05
ENSG00000112852	PCDHB2	−1.24855528	0.002868391
ENSG00000123096	SSPN	−1.248840998	3.34177E−07
ENSG00000088882	CPXM1	−1.249480083	1.16543E−05
ENSG00000173369	C1QB	−1.250210526	0.000370687
ENSG00000157927	RADIL	−1.250353421	4.99087E−05
ENSG00000134138	MEIS2	−1.250579671	4.12937E−06
ENSG00000176971	FIBIN	−1.250818033	7.09634E−06
ENSG00000143867	OSR1	−1.250847091	0.002687218
ENSG00000196990	FAM163B	−1.251514865	0.005702874
ENSG00000012779	ALOX5	−1.251558885	9.25031E−06
ENSG00000277632	CCL3	−1.251852795	0.001088763
ENSG00000259030	FPGT-TNNI3K	−1.252099756	7.79554E−05
ENSG00000121904	CSMD2	−1.252642618	5.72693E−05
ENSG00000168995	SIGLEC7	−1.253049397	0.000211989
ENSG00000042781	USH2A	−1.254282147	0.012941087
ENSG00000012124	CD22	−1.25449932	6.46719E−05
ENSG00000106952	TNFSF8	−1.255518784	0.000342742
ENSG00000198832	SELM	−1.256701248	1.32513E−06
ENSG00000103196	CRISPLD2	−1.256801651	3.81028E−05
ENSG00000182511	FES	−1.257683426	4.16362E−06
ENSG00000161681	SHANK1	−1.258360578	6.70875E−06
ENSG00000169896	ITGAM	−1.258921389	4.44127E−06
ENSG00000101336	HCK	−1.258973841	2.82361E−06
ENSG00000131080	EDA2R	−1.259179161	0.000177705
ENSG00000138685	FGF2	−1.259243723	0.000405516
ENSG00000130592	LSP1	−1.259748483	1.66007E−06
ENSG00000186642	PDE2A	−1.260719144	0.000143239
ENSG00000158714	SLAMF8	−1.260731734	2.10135E−05
ENSG00000171408	PDE7B	−1.26081495	0.000733498
ENSG00000139194	RBP5	−1.262108874	0.01202083
ENSG00000175040	CHST2	−1.26369885	2.11475E−08
ENSG00000000971	CFH	−1.26436294	0.0018355
ENSG00000128284	APOL3	−1.265295833	5.82398E−06
ENSG00000101134	DOK5	−1.266010005	1.35482E−06
ENSG00000163453	IGFBP7	−1.267085411	4.16105E−06
ENSG00000073282	TP63	−1.267574404	0.000793904
ENSG00000143382	ADAMTSL4	−1.268399388	6.51103E−06
ENSG00000061455	PRDM6	−1.268515966	1.40843E−06
ENSG00000170153	RNF150	−1.26878095	8.00283E−05
ENSG00000156127	BATF	−1.268835188	4.98746E−05
ENSG00000131849	ZNF132	−1.268912419	1.44968E−05
ENSG00000050165	DKK3	−1.269658216	3.16481E−05
ENSG00000128573	FOXP2	−1.270199233	0.002865004
ENSG00000153822	KCNJ16	−1.270927062	0.009894448
ENSG00000171310	CHST11	−1.271667281	7.67678E−07
ENSG00000129946	SHC2	−1.27191939	1.20582E−05
ENSG00000110077	MS4A6A	−1.272018639	8.02783E−05
ENSG00000110887	DAO	−1.272940567	0.038705581
ENSG00000135604	STX11	−1.27362525	2.34861E−05
ENSG00000143127	ITGA10	−1.27434303	1.63616E−05
ENSG00000131378	RFTN1	−1.275036452	1.03636E−07
ENSG00000005471	ABCB4	−1.27504517	0.021354689
ENSG00000088827	SIGLEC1	−1.275248866	0.001161319
ENSG00000133048	CHI3L1	−1.275930342	0.015476928
ENSG00000101082	SLA2	−1.276914495	5.66399E−05
ENSG00000133561	GIMAP6	−1.277080684	1.27047E−05

TABLE 3A-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000167601	AXL	−1.277150996	6.21921E−07
ENSG00000151726	ACSL1	−1.277649272	0.000179175
ENSG00000048052	HDAC9	−1.27780238	7.38287E−06
ENSG00000172915	NBEA	−1.279100707	8.58737E−05
ENSG00000106571	GLI3	−1.279119677	6.37669E−06
ENSG00000142347	MYO1F	−1.280247206	2.33821E−07
ENSG00000154263	ABCA10	−1.280275968	7.79115E−06
ENSG00000105639	JAK3	−1.280516459	2.37869E−06
ENSG00000060718	COL11A1	−1.280755681	0.000473859
ENSG00000184347	SLIT3	−1.280859693	1.87622E−05
ENSG00000163154	TNFAIP8L2	−1.281119032	6.24608E−06
ENSG00000231389	HLA-DPA1	−1.281151326	3.98236E−05
ENSG00000180353	HCLS1	−1.281208272	9.14566E−07
ENSG00000169403	PTAFR	−1.281319195	1.21654E−06
ENSG00000145075	CCDC39	−1.281457227	0.004113882
ENSG00000007372	PAX6	−1.281666878	0.011434259
ENSG00000123685	BATF3	−1.281698919	8.73266E−07
ENSG00000103449	SALL1	−1.281808222	0.048202618
ENSG00000122223	CD244	−1.281817741	0.001575787
ENSG00000151067	CACNA1C	−1.283399954	1.82887E−06
ENSG00000160326	SLC2A6	−1.283525121	4.61249E−06
ENSG00000169442	CD52	−1.283852449	3.13843E−05
ENSG00000143869	GDF7	−1.283939364	0.002159459
ENSG00000188906	LRRK2	−1.284364899	4.34378E−05
ENSG00000073712	FERMT2	−1.285060092	1.26489E−06
ENSG00000164691	TAGAP	−1.285333766	2.05026E−05
ENSG00000023902	PLEKHO1	−1.285698986	8.75035E−08
ENSG00000173198	CYSLTR1	−1.286982597	0.000173899
ENSG00000107249	GLIS3	−1.287570918	1.97989E−06
ENSG00000155926	SLA	−1.287799377	1.57852E−05
ENSG00000173068	BNC2	−1.288356134	7.97644E−06
ENSG00000182636	NDN	−1.289091341	2.2782E−05
ENSG00000214063	TSPAN4	−1.289501439	1.55933E−06
ENSG00000145147	SLIT2	−1.290042287	1.65513E−06
ENSG00000118308	LRMP	−1.290771912	0.000145328
ENSG00000146674	IGFBP3	−1.291303554	1.84669E−05
ENSG00000274618	HIST1H4F	−1.292844217	0.000531384
ENSG00000165457	FOLR2	−1.294061611	0.008304119
ENSG00000121297	TSHZ3	−1.294305445	6.01962E−08
ENSG00000244486	SCARF2	−1.294334674	1.4429E−07
ENSG00000099958	DERL3	−1.294783854	0.000580699
ENSG00000169992	NLGN2	−1.295120775	6.53704E−07
ENSG00000138378	STAT4	−1.29543975	1.19766E−05
ENSG00000171502	COL24A1	−1.295886151	9.38941E−05
ENSG00000053524	MCF2L2	−1.296416705	4.61249E−06
ENSG00000165246	NLGN4Y	−1.296638324	0.031538531
ENSG00000188517	COL25A1	−1.297150023	0.004307607
ENSG00000168542	COL3A1	−1.297227553	7.74067E−06
ENSG00000130222	GADD45G	−1.297476279	0.000261918
ENSG00000160255	ITGB2	−1.297511297	3.95752E−06
ENSG00000154654	NCAM2	−1.297833226	0.000573734
ENSG00000065320	NTN1	−1.299325227	0.011148482
ENSG00000177575	CD163	−1.299893086	0.000390015
ENSG00000117245	KIF17	−1.300534329	0.000200591
ENSG00000276231	PIK3R6	−1.300549794	1.91479E−07
ENSG00000160801	PTH1R	−1.302062097	0.003466999
ENSG00000086730	LAT2	−1.302433939	2.31493E−07
ENSG00000197471	SPN	−1.302532526	1.74498E−06
ENSG00000140009	ESR2	−1.30293787	0.005107637
ENSG00000242732	RGAG4	−1.303090886	5.61793E−06
ENSG00000126264	HCST	−1.30343371	0.00015882
ENSG00000198400	NTRK1	−1.303453983	0.002234139
ENSG00000074706	IPCEF1	−1.303676007	0.000105006
ENSG00000164483	SAMD3	−1.304642308	3.69683E−05
ENSG00000154330	PGM5	−1.304850142	0.01764485
ENSG00000179542	SLITRK4	−1.305385651	0.00073584
ENSG00000138722	MMRN1	−1.305607805	0.019467695
ENSG00000172575	RASGRP1	−1.305665733	6.38526E−06
ENSG00000120820	GLT8D2	−1.306404154	3.59864E−06
ENSG00000025708	TYMP	−1.306791046	6.88891E−06
ENSG00000135914	HTR2B	−1.306928718	0.000742508
ENSG00000018869	ZNF582	−1.307031585	7.55275E−05
ENSG00000182578	CSF1R	−1.308063603	7.89301E−07
ENSG00000128652	HOXD3	−1.308428032	0.042593636
ENSG00000041515	MYO16	−1.309271715	0.004238641

TABLE 3A-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000115468	EFHD1	−1.3097124	3.0664E−06
ENSG00000177706	FAM20C	−1.310293141	3.86458E−07
ENSG00000142494	SLC47A1	−1.310742871	0.000442139
ENSG00000204936	CD177	−1.311062655	0.00137739
ENSG00000066336	SPI1	−1.311466097	5.07593E−07
ENSG00000144648	ACKR2	−1.311541006	7.51745E−05
ENSG00000125910	S1PR4	−1.311857708	0.000280538
ENSG00000167711	SERPINF2	−1.312573286	0.027314297
ENSG00000110876	SELPLG	−1.312992457	1.09675E−06
ENSG00000181631	P2RY13	−1.313224407	8.50524E−05
ENSG00000160408	ST6GALNAC6	−1.313444839	1.89078E−09
ENSG00000172935	MRGPRF	−1.314382734	1.97624E−06
ENSG00000171246	NPTX1	−1.31515225	0.00010151
ENSG00000090534	THPO	−1.315369162	0.003521046
ENSG00000091106	NLRC4	−1.315628669	3.0764E−05
ENSG00000166448	TMEM130	−1.316288618	0.001135103
ENSG00000141505	ASGR1	−1.316625086	0.044561092
ENSG00000149294	NCAM1	−1.317114455	0.000253712
ENSG00000125508	SRMS	−1.317996432	0.024352628
ENSG00000173200	PARP15	−1.31871982	5.34552E−05
ENSG00000112303	VNN2	−1.318751662	0.000188548
ENSG00000111860	CEP85L	−1.319376477	2.62136E−06
ENSG00000104903	LYL1	−1.319477213	2.23061E−07
ENSG00000132837	DMGDH	−1.320758807	0.020816064
ENSG00000171649	ZIK1	−1.320964286	3.70539E−06
ENSG00000206190	ATP10A	−1.321006994	4.38137E−07
ENSG00000257242	C120rf79	−1.321305486	0.000907887
ENSG00000046889	PREX2	−1.322313956	3.43678E−07
ENSG00000198502	HLA-DRB5	−1.322986017	0.000541791
ENSG00000152217	SETBP1	−1.323499748	3.31931E−06
ENSG00000170390	DCLK2	−1.324259917	3.23652E−07
ENSG00000179144	GIMAP7	−1.324311921	5.65388E−05
ENSG00000136574	GATA4	−1.325975478	0.002098347
ENSG00000133687	TMTC1	−1.32598008	1.33594E−05
ENSG00000175899	A2M	−1.32658222	8.69517E−05
ENSG00000169515	CCDC8	−1.327236999	1.33243E−05
ENSG00000152137	HSPB8	−1.327754381	1.69986E−06
ENSG00000122679	RAMP3	−1.328515607	2.83652E−05
ENSG00000107485	GATA3	−1.328554159	0.000155867
ENSG00000260314	MRC1	−1.328988195	0.000176206
ENSG00000183801	OLFML1	−1.329281354	7.5462E−06
ENSG00000206432	TMEM200C	−1.329441229	1.62807E−05
ENSG00000111863	ADTRP	−1.329916534	0.000158492
ENSG00000269948	RP11-248J23.6	−1.330372451	1.78916E−06
ENSG00000079102	RUNX1T1	−1.330528167	1.26528E−06
ENSG00000135502	SLC26A10	−1.331173412	3.67599E−05
ENSG00000181444	ZNF467	−1.33136971	7.70788E−06
ENSG00000089041	P2RX7	−1.331483229	3.42517E−07
ENSG00000167083	GNGT2	−1.331616205	5.65388E−05
ENSG00000111186	WNT5B	−1.332259291	0.00800442
ENSG00000135439	AGAP2	−1.333217564	8.29471E−06
ENSG00000091844	RGS17	−1.333570377	0.00046005
ENSG00000083814	ZNF671	−1.333785964	1.76507E−05
ENSG00000185046	ANKS1B	−1.334046718	0.003477125
ENSG00000170955	PRKCDBP	−1.334151626	7.548E−07
ENSG00000239713	APOBEC3G	−1.334850049	4.0212E−05
ENSG00000144152	FBLN7	−1.335334356	4.4053E−07
ENSG00000125144	MT1G	−1.335609178	0.016611049
ENSG00000119535	CSF3R	−1.336845559	6.53044E−06
ENSG00000142512	SIGLEC10	−1.337447232	1.20046E−05
ENSG00000112619	PRPH2	−1.33866708	2.87088E−06
ENSG00000088881	EBF4	−1.339348505	5.38866E−07
ENSG00000163884	KLF15	−1.339432665	0.014437879
ENSG00000144619	CNTN4	−1.339647048	2.60728E−06
ENSG00000109625	CPZ	−1.343177158	0.002327224
ENSG00000168994	PXDC1	−1.344912997	4.38273E−06
ENSG00000136630	HLX	−1.345021844	2.11475E−08
ENSG00000164935	DCSTAMP	−1.345718397	0.00099329
ENSG00000139329	LUM	−1.346025378	2.08379E−05
ENSG00000178343	SHISA3	−1.346216604	3.25415E−05
ENSG00000154175	ABI3BP	−1.347094852	2.44453E−05
ENSG00000111341	MGP	−1.347287081	0.000167446
ENSG00000073146	MOV10L1	−1.347343511	2.87088E−06
ENSG00000163751	CPA3	−1.347495163	0.000471133
ENSG00000092607	TBX15	−1.347502849	0.009330017

TABLE 3A-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000156218	ADAMTSL3	−1.347800829	0.00065811
ENSG00000166501	PRKCB	−1.347966306	4.88776E−06
ENSG00000106809	OGN	−1.348866721	0.04030366
ENSG00000049089	COL9A2	−1.349039206	0.000477145
ENSG00000166831	RBPMS2	−1.349104821	5.79938E−06
ENSG00000104972	LILRB1	−1.349256104	3.17927E−06
ENSG00000071575	TRIB2	−1.349463531	8.48499E−08
ENSG00000204851	PNMAL2	−1.349510321	2.16739E−05
ENSG00000186517	ARHGAP30	−1.34999955	3.42653E−08
ENSG00000131355	EMR3	−1.351019854	0.000162246
ENSG00000151322	NPAS3	−1.351096064	0.002700003
ENSG00000204577	LILRB3	−1.351489569	1.06562E−05
ENSG00000187688	TRPV2	−1.351689403	1.03618E−07
ENSG00000120217	CD274	−1.352018951	0.000186348
ENSG00000130303	BST2	−1.352200439	3.55771E−05
ENSG00000187955	COL14A1	−1.352408958	1.70562E−05
ENSG00000198795	ZNF521	−1.352652582	2.66038E−06
ENSG00000136305	CIDEB	−1.352905676	1.41945E−05
ENSG00000185518	SV2B	−1.352927982	0.001480163
ENSG00000034053	APBA2	−1.353722727	5.87163E−05
ENSG00000158008	EXTL1	−1.35435216	0.000116194
ENSG00000198753	PLXNB3	−1.356290561	0.00942131
ENSG00000075884	ARHGAP15	−1.357759474	4.15343E−07
ENSG00000232653	GOLGA8N	−1.358202793	6.87665E−06
ENSG00000105825	TFPI2	−1.359265276	0.007582781
ENSG00000143028	SYPL2	−1.360179735	4.64967E−05
ENSG00000137203	TFAP2A	−1.360200468	0.007854124
ENSG00000179921	GPBAR1	−1.360454991	7.36894E−06
ENSG00000151789	ZNF385D	−1.361677353	0.000281211
ENSG00000139174	PRICKLE1	−1.362285328	9.96917E−07
ENSG00000137727	ARHGAP20	−1.363402347	0.000268589
ENSG00000111087	GLI1	−1.363950949	6.93396E−07
ENSG00000204482	LST1	−1.36411559	7.66626E−06
ENSG00000185736	ADARB2	−1.364256843	0.008092941
ENSG00000203710	CR1	−1.364350738	9.04798E−05
ENSG00000107984	DKK1	−1.364586457	0.011140226
ENSG00000186310	NAP1L3	−1.365077229	3.65785E−05
ENSG00000196090	PTPRT	−1.365704215	0.002284951
ENSG00000131042	LILRB2	−1.367205569	1.96556E−05
ENSG00000007174	DNAH9	−1.367394384	0.002900476
ENSG00000079263	SP140	−1.36785107	1.3134E−05
ENSG00000119681	LTBP2	−1.368127362	6.10597E−06
ENSG00000141052	MYOCD	−1.36854398	3.04178E−05
ENSG00000151948	GLT1D1	−1.369184391	0.00319049
ENSG00000147576	ADHFE1	−1.369743451	0.000415856
ENSG00000147100	SLC16A2	−1.369747445	2.96438E−05
ENSG00000124212	PTGIS	−1.369922229	2.13007E−05
ENSG00000130203	APOE	−1.369948171	0.000177552
ENSG00000111058	ACSS3	−1.370093223	0.000199953
ENSG00000167483	FAM129C	−1.370153299	0.003804528
ENSG00000130584	ZBTB46	−1.37104526	9.733E−08
ENSG00000109339	MAPK10	−1.37213797	3.86458E−07
ENSG00000184838	PRR16	−1.372651407	8.57424E−07
ENSG00000183813	CCR4	−1.373417547	2.99849E−05
ENSG00000174123	TLR10	−1.373495023	0.000719912
ENSG00000148346	LCN2	−1.377542448	0.011442001
ENSG00000111181	SLC6A12	−1.378635316	0.000474755
ENSG00000112320	SOBP	−1.378774929	2.34766E−05
ENSG00000184371	CSF1	−1.379520207	7.07184E−08
ENSG00000170500	LONRF2	−1.379602914	0.020055703
ENSG00000100842	EFS	−1.37976028	4.72689E−07
ENSG00000120457	KCNJ5	−1.380906549	3.40174E−05
ENSG00000163629	PTPN13	−1.381887352	5.61759E−05
ENSG00000159261	CLDN14	−1.382221288	0.002563638
ENSG00000125730	C3	−1.382364557	0.019656541
ENSG00000136732	GYPC	−1.382700631	6.76163E−07
ENSG00000069535	MAOB	−1.382763003	0.000708729
ENSG00000125869	LAMP5	−1.382937902	3.0356E−05
ENSG00000181847	TIGIT	−1.383017285	0.000127192
ENSG00000055955	ITIH4	−1.384463334	0.011239072
ENSG00000158786	PLA2G2F	−1.38452622	0.002641231
ENSG00000171303	KCNK3	−1.385123011	0.001069729
ENSG00000163431	LMOD1	−1.386020175	4.26452E−07
ENSG00000173208	ABCD2	−1.386459547	0.001643421
ENSG00000126882	FAM78A	−1.387007814	1.32024E−07

TABLE 3A-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000275302	CCL4	−1.387251557	4.6769E−05
ENSG00000184922	FMNL1	−1.387597199	1.07962E−07
ENSG00000163599	CTLA4	−1.387607292	0.00268844
ENSG00000082175	PGR	−1.389867437	3.57778E−07
ENSG00000223865	HLA-DPB1	−1.391952069	7.01003E−06
ENSG00000019991	HGF	−1.39215834	4.72444E−05
ENSG00000006638	TBXA2R	−1.392218154	1.24432E−06
ENSG00000149090	PAMR1	−1.392251281	8.90555E−06
ENSG00000105419	MEIS3	−1.394935236	1.50003E−08
ENSG00000170458	CD14	−1.395154873	3.42103E−05
ENSG00000105426	PTPRS	−1.396136464	7.90124E−07
ENSG00000099769	IGFALS	−1.39841302	0.014093131
ENSG00000196724	ZNF418	−1.398478329	2.47697E−06
ENSG00000164344	KLKB1	−1.399527697	0.008139283
ENSG00000205403	CFI	−1.400491941	0.000225745
ENSG00000198670	LPA	−1.400790691	0.037679104
ENSG00000015285	WAS	−1.40095576	1.28669E−06
ENSG00000171451	DSEL	−1.401184119	7.25095E−07
ENSG00000211448	DIO2	−1.402743681	0.00099329
ENSG00000157168	NRG1	−1.403108401	0.017067172
ENSG00000131203	IDO1	−1.403413305	0.023073967
ENSG00000117560	FASLG	−1.40413241	0.001541034
ENSG00000180509	KCNE1	−1.404776361	0.000350888
ENSG00000196557	CACNA1H	-1.406476726	4.86586E−07
ENSG00000139344	AMDHD1	−1.406623034	0.031688173
ENSG00000143297	FCRL5	−1.40681718	0.007995403
ENSG00000182162	P2RY8	−1.408331696	2.37136E−06
ENSG00000204103	MAFB	−1.409430633	7.71039E−08
ENSG00000171476	HOPX	−1.410188178	2.62136E−06
ENSG00000106991	ENG	−1.410800156	4.1422E−08
ENSG00000180155	LYNX1	−1.410808547	0.000131545
ENSG00000244482	LILRA6	−1.410838552	4.93995E−05
ENSG00000113209	PCDHB5	−1.410935916	0.000570709
ENSG00000188641	DPYD	−1.41099067	1.26489E−06
ENSG00000162576	MXRA8	−1.411211889	2.92985E−06
ENSG00000187824	TMEM220	−1.412792849	0.000151776
ENSG00000159212	CLIC6	−1.413294685	0.002501545
ENSG00000183484	GPR132	-1.413513868	4.12937E−06
ENSG00000091986	CCDC80	−1.413746341	1.5288E−05
ENSG00000125735	TNFSFI4	-1.414431004	0.001728779
ENSG00000163520	FBLN2	−1.415408525	1.56411E−07
ENSG00000174807	CD248	−1.415713111	5.97701E−08
ENSG00000100055	CYTH4	−1.416880465	1.20416E−07
ENSG00000188536	HBA2	−1.417836366	0.000364417
ENSG00000104894	CD37	−1.418932735	2.94372E−06
ENSG00000142156	COL6A1	−1.419394887	3.57778E−07
ENSG00000107736	CDH23	−1.419845685	2.48367E−06
ENSG00000177807	KCNJ10	−1.420156049	0.003561478
ENSG00000168546	GFRA2	−1.420256336	0.007027914
ENSG00000007237	GAS7	−1.420426969	7.11386E−08
ENSG00000176928	GCNT4	−1.421597699	1.20461E−06
ENSG00000115594	IL1R1	−1.421732637	6.55067E−07
ENSG00000153253	SCN3A	−1.422622063	0.004076984
ENSG00000177875	CCDC184	-1.422806829	6.80303E−06
ENSG00000102452	NALCN	−1.423964742	9.44593E−06
ENSG00000165507	C10orf10	−1.424175818	2.67921E−06
ENSG00000112139	MDGA1	−1.424370102	1.1552E−05
ENSG00000122367	LDB3	−1.425971299	0.000635937
ENSG00000133246	PRAM1	−1.427538999	1.13171E−07
ENSG00000106624	AEBP1	−1.427665793	2.90319E−05
ENSG00000196735	HLA-DQA1	−1.427729423	0.000109363
ENSG00000180096	SEPT1	−1.428104072	3.14232E−06
ENSG00000188305	C19orf35	−1.429967092	9.02335E−05
ENSG00000179593	ALOX15B	-1.43061843	0.001063826
ENSG00000113594	LIFR	−1.430655583	0.002521619
ENSG00000127124	HIVEP3	−1.432113664	5.9378E−07
ENSG00000198771	RCSD1	−1.433589871	3.75075E−08
ENSG00000162676	GFI1	−1.434153621	1.93745E−05
ENSG00000142303	ADAMTS10	-1.434246952	3.42653E−08
ENSG00000143816	WNT9A	−1.436038799	8.14408E−06
ENSG00000204161	C10orf128	−1.436084505	2.10218E−06
ENSG00000091592	NLRP1	−1.436094337	8.17503E−07
ENSG00000188015	S100A3	−1.436569384	0.000896234
ENSG00000136490	LIMD2	−1.436957681	4.79665E−07
ENSG00000093134	VNN3	−1.439618817	0.003014081

TABLE 3A-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000128815	WDFY4	−1.440484646	3.34177E−07
ENSG00000115226	FNDC4	−1.441984776	7.15723E−05
ENSG00000104415	WISP1	−1.442348917	1.42448E−06
ENSG00000153404	PLEKHG4B	−1.442485316	0.003493783
ENSG00000130208	APOC1	−1.443020777	0.003780691
ENSG00000182195	LDOC1	−1.445187497	1.69986E−06
ENSG00000178562	CD28	−1.446037961	7.08224E−05
ENSG00000162551	ALPL	−1.446724779	0.002006821
ENSG00000177989	ODF3B	−1.44701482	3.16493E−07
ENSG00000138080	EMILIN1	−1.449660676	3.86458E−07
ENSG00000169946	ZFPM2	−1.45014781	2.26549E−07
ENSG00000227507	LTB	−1.452433452	0.000139002
ENSG00000166676	TVP23A	−1.452869264	1.12963E−05
ENSG00000011028	MRC2	−1.452971353	5.97701E−08
ENSG00000100385	IL2RB	−1.453413248	2.49212E−06
ENSG00000007933	FMO3	−1.453747592	0.000546202
ENSG00000110665	C11orf21	−1.453900259	0.001654857
ENSG00000078295	ADCY2	−1.454015822	0.00117231
ENSG00000129450	SIGLEC9	−1.454866574	1.19976E−07
ENSG00000186891	TNFRSF18	−1.455068405	8.02058E−05
ENSG00000185070	FLRT2	−1.455496456	3.37022E−07
ENSG00000144596	GRIP2	−1.455568908	5.08238E−05
ENSG00000263961	C1orf186	−1.456739139	7.53646E−05
ENSG00000138315	OIT3	−1.456783399	0.01233807
ENSG00000107562	CXCL12	−1.45719748	0.000157736
ENSG00000184408	KCND2	−1.458804262	1.05224E−05
ENSG00000009694	TENM1	−1.459308234	0.010433276
ENSG00000163606	CD200R1	−1.459667858	0.000147918
ENSG00000250510	GPR162	−1.46050917	4.28987E−06
ENSG00000123843	C4BPB	−1.461529734	0.000179871
ENSG00000168874	ATOH8	−1.461785258	0.01863606
ENSG00000182771	GRID1	−1.462063879	0.000131466
ENSG00000143851	PTPN7	−1.462663503	7.79115E−06
ENSG00000070190	DAPP1	−1.463152553	2.05078E−05
ENSG00000105851	PIK3CG	−1.463748694	3.82695E−08
ENSG00000160013	PTGIR	−1.463858823	7.38276E−07
ENSG00000142173	COL6A2	−1.464505224	6.80791E−07
ENSG00000105609	LILRB5	−1.464802202	0.004137589
ENSG00000176293	ZNF135	−1.464846766	3.89986E−06
ENSG00000109794	FAM149A	−1.465397328	2.06106E−05
ENSG00000137672	TRPC6	−1.465736331	1.57852E−05
ENSG00000158270	COLEC12	−1.46579545	0.000307779
ENSG00000143515	ATP8B2	−1.465958032	2.11475E−08
ENSG00000188153	COL4A5	−1.466509884	1.37202E−05
ENSG00000141506	PIK3R5	−1.46752066	3.57627E−07
ENSG00000122122	SASH3	−1.468149185	1.14871E−07
ENSG00000141469	SLC14A1	−1.469695897	0.013631147
ENSG00000234465	PINLYP	−1.470357295	9.14566E−07
ENSG00000116194	ANGPTL1	−1.471124132	0.000718491
ENSG00000111913	FAM65B	−1.471340117	2.21816E−06
ENSG00000122877	EGR2	−1.473373856	8.6066E−07
ENSG00000096996	IL12RB1	−1.476435937	1.56632E−06
ENSG00000132329	RAMP1	−1.477056239	3.65341E−06
ENSG00000146555	SDK1	−1.477506838	5.90996E−05
ENSG00000132274	TRIM22	−1.47813492	1.61701E−06
ENSG00000116132	PRRX1	−1.478614381	5.83943E−05
ENSG00000185739	SRL	−1.47907594	0.000232338
ENSG00000165072	MAMDC2	−1.479375871	0.002441418
ENSG00000100024	UPB1	−1.479500636	0.01373858
ENSG00000169862	CTNND2	−1.479738121	0.001140847
ENSG00000112182	BACH2	−1.480035707	1.9412E−07
ENSG00000132321	IQCA1	−1.480413044	4.15713E−05
ENSG00000180644	PRF1	−1.481514029	0.000691017
ENSG00000144712	CAND2	−1.48205596	0.000115084
ENSG00000198963	RORB	−1.483142457	0.001261372
ENSG00000171777	RASGRP4	−1.484499328	3.86458E−07
ENSG00000166546	BEAN1	−1.486354863	0.00021393
ENSG00000160654	CD3G	−1.48798618	1.05447E−05
ENSG00000188820	FAM26F	−1.48936868	0.000221408
ENSG00000168421	RHOH	−1.490154237	3.62887E−06
ENSG00000146938	NLGN4X	−1.491016537	8.90555E−06
ENSG00000196405	EVL	−1.492261635	7.33986E−08
ENSG00000116690	PRG4	−1.492579766	0.011600499
ENSG00000213203	GIMAP1	−1.494333415	4.7121E−06
ENSG00000049540	ELN	−1.494537514	4.9683E−06

TABLE 3A-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000140287	HDC	−1.495638222	4.0389E−05
ENSG00000181790	BAI1	−1.49727332	0.000174264
ENSG00000168875	SOX14	−1.498521925	0.015329029
ENSG00000166741	NNMT	−1.499407723	9.12715E−05
ENSG00000168140	VASN	−1.500069865	2.3508E−08
ENSG00000124256	ZBP1	−1.501827474	8.46724E−05
ENSG00000136244	IL6	−1.502133365	0.00018496
ENSG00000211445	GPX3	−1.502476421	7.44696E−05
ENSG00000111796	KLRB1	−1.503537324	0.001140171
ENSG00000111452	GPR133	−1.504413354	7.32874E−07
ENSG00000130224	LRCH2	−1.505032102	7.99716E−05
ENSG00000072163	LIMS2	−1.505234356	1.86227E−08
ENSG00000173762	CD7	−1.507000954	0.000639191
ENSG00000106327	TFR2	−1.507799563	0.015023864
ENSG00000101445	PPP1R16B	−1.508082577	9.93664E−07
ENSG00000183549	ACSM5	−1.508248292	0.011197472
ENSG00000154277	UCHL1	−1.5087134	1.69988E−05
ENSG00000105369	CD79A	−1.509321396	0.000240457
ENSG00000174348	PODN	−1.509428102	5.35127E−07
ENSG00000134201	GSTM5	−1.509980041	2.05026E−05
ENSG00000140274	DUOXA2	−1.510700006	0.007182098
ENSG00000197943	PLCG2	−1.510731018	2.11475E−08
ENSG00000091656	ZFHX4	−1.510945405	7.68702E−06
ENSG00000104974	LILRA1	−1.512817854	2.4424E−05
ENSG00000013725	CD6	−1.513688335	3.65773E−06
ENSG00000176533	GNG7	−1.514775354	1.50099E−06
ENSG00000162692	VCAM1	−1.515374623	2.18735E−06
ENSG00000054938	CHRDL2	−1.51790575	0.005020885
ENSG00000187260	WDR86	−1.517998511	3.2638E−06
ENSG00000138696	BMPR1B	−1.519879182	4.77818E−05
ENSG00000100368	CSF2RB	−1.520882383	7.71039E−08
ENSG00000161405	IKZF3	−1.524231413	1.40958E−05
ENSG00000165125	TRPV6	−1.524418345	0.006282434
ENSG00000188404	SELL	−1.524526012	1.67292E−05
ENSG00000131634	TMEM204	−1.527418737	7.67289E−09
ENSG00000115604	IL18R1	−1.527507371	2.06106E−05
ENSG00000184226	PCDH9	−1.527583929	4.10717E−07
ENSG00000162739	SLAMF6	−1.528926599	5.63686E−05
ENSG00000074047	GLI2	−1.529208704	5.88447E−09
ENSG00000104332	SFRP1	−1.529634224	8.34178E−06
ENSG00000275395	FCGBP	−1.529686158	0.002214567
ENSG00000072694	FCGR2B	−1.531458196	7.92606E−06
ENSG00000153563	CD8A	−1.531510557	1.70823E−05
ENSG00000235098	ANKRD65	−1.532017749	9.38941E−05
ENSG00000138964	PARVG	−1.533014221	1.03618E−07
ENSG00000171444	MCC	−1.533092846	1.65611E−06
ENSG00000044524	EPHA3	−1.534789634	1.26977E−06
ENSG00000110324	IL10RA	−1.535684867	1.19976E−07
ENSG00000149527	PLCH2	−1.540087018	5.02948E−06
ENSG00000134853	PDGFRA	−1.541650809	2.93382E−06
ENSG00000115602	IL1RL1	−1.543852151	0.000336124
ENSG00000072840	EVC	−1.546053845	2.11475E−08
ENSG00000188385	JAKMIP3	−1.548233697	1.65301E−06
ENSG00000017427	IGF1	−1.548256962	0.000769952
ENSG00000167261	DPEP2	−1.548790353	9.47397E−08
ENSG00000139800	ZIC5	−1.549320247	0.007504945
ENSG00000163071	SPATA18	−1.550345627	1.95046E−06
ENSG00000020633	RUNX3	−1.55042504	1.67438E−08
ENSG00000244731	C4A	−1.550464023	0.005818325
ENSG00000122691	TWIST1	−1.551224176	0.00039783
ENSG00000138061	CYP1B1	−1.551931643	2.4673E−06
ENSG00000094755	GABRP	−1.552008805	0.007818468
ENSG00000064300	NGFR	−1.553953529	6.5295E−05
ENSG00000172817	CYP7B1	−1.554195748	1.26489E−06
ENSG00000005102	MEOX1	−1.554438791	0.000130756
ENSG00000179348	GATA2	−1.556681027	4.6063E−06
ENSG00000171608	PIK3CD	−1.558634197	3.7402E−08
ENSG00000129993	CBFA2T3	−1.55949201	1.78916E−06
ENSG00000122188	LAX1	−1.562512852	0.000209843
ENSG00000136155	SCEL	−1.563969201	0.008172459
ENSG00000156222	SLC28A1	−1.565856008	0.021093744
ENSG00000179583	CIITA	−1.56914011	2.47492E−06
ENSG00000148053	NTRK2	−1.569472794	0.001412759
ENSG00000179344	HLA-DQB1	−1.57087044	4.99227E−05
ENSG00000108950	FAM20A	−1.571607534	4.3045E−05

TABLE 3A-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000183287	CCBE1	−1.571882164	2.15791E−05
ENSG00000115607	IL18RAP	−1.57397144	0.000340421
ENSG00000149131	SERPING1	−1.574477195	6.28766E−05
ENSG00000018625	ATP1A2	−1.574584571	0.000677893
ENSG00000160282	FTCD	−1.576568217	0.045728705
ENSG00000115523	GNLY	−1.577209668	0.000358699
ENSG00000130812	ANGPTL6	−1.577413446	0.000176276
ENSG00000100628	ASB2	−1.578587567	3.93982E−05
ENSG00000126603	GL1S2	−1.578644116	5.47145E−08
ENSG00000162894	FAIM3	−1.578890821	1.25594E−05
ENSG00000203805	PPAPDC1A	−1.579129572	7.66724E−05
ENSG00000123360	PDE1B	−1.580223798	1.27701E−07
ENSG00000050730	TNIP3	−1.580726231	0.000100104
ENSG00000243696	RPS-966M1.6	−1.580785901	0.002853316
ENSG00000141431	ASXL3	−1.581098614	3.19022E−05
ENSG00000253304	TMEM200B	−1.583600932	3.7402E−08
ENSG00000115648	MLPH	−1.584496312	8.46724E−05
ENSG00000182463	TSHZ2	−1.585228768	1.51929E−07
ENSG00000145708	CRHBP	−1.586345108	0.02136514
ENSG00000139547	RDH16	−1.587228603	0.005684036
ENSG00000117215	PLA2G2D	−1.587484636	0.014025318
ENSG00000101463	SYNDIG1	−1.58750882	0.0001669
ENSG00000187193	MT1X	−1.587516155	0.002355558
ENSG00000127528	KLF2	−1.588749817	3.42653E−08
ENSG00000007908	SELE	−1.591517313	0.003609117
ENSG00000187479	C11orf96	−1.59175367	5.33407E−06
ENSG00000110448	CD5	−1.593521292	2.70401E−05
ENSG00000101825	MXRA5	−1.593583615	3.09227E−05
ENSG00000177098	SCN4B	−1.594088271	5.71046E−05
ENSG00000144681	STAC	−1.594603568	0.000191125
ENSG00000138311	ZNF365	−1.595470841	1.67571E−05
ENSG00000077942	FBLN1	−1.596319762	0.002377355
ENSG00000169083	AR	−1.597168407	0.00095126
ENSG00000146192	FGD2	−1.597387366	1.67438E−08
ENSG00000078589	P2RY10	−1.597696437	0.000116257
ENSG00000179388	EGR3	−1.597852607	3.28506E−06
ENSG00000174944	P2RY14	−1.60050109	3.46148E−05
ENSG00000005844	ITGAL	−1.601350362	4.54336E−07
ENSG00000172215	CXCR6	−1.602020984	6.66974E−05
ENSG00000104435	STMN2	−1.602700919	0.000840704
ENSG00000186479	RGS7BP	−1.603707527	0.000105798
ENSG00000153976	HS3ST3A1	−1.604351934	8.32817E−06
ENSG00000150051	MKX	−1.605162917	3.39392E−05
ENSG00000106483	SFRP4	−1.605254889	2.10734E−05
ENSG00000105374	NKG7	−1.60525897	0.000512273
ENSG00000002746	HECW1	−1.605297814	1.39095E−05
ENSG00000149970	CNKSR2	−1.607381055	1.80011E−05
ENSG00000157103	SLC6A1	−1.607433083	1.47296E−05
ENSG00000142871	CYR61	−1.607445176	1.33133E−05
ENSG00000196329	GIMAP5	−1.608196974	4.38102E−05
ENSG00000161544	CYGB	−1.608829885	2.00477E−07
ENSG00000132386	SERPINF1	−1.609846768	5.04228E−06
ENSG00000073754	CD5L	−1.610830571	0.031773904
ENSG00000080007	DDX43	−1.611173367	0.001214143
ENSG00000162804	SNED1	−1.611865848	5.42959E−08
ENSG00000145864	GABRB2	−1.614793569	0.036956319
ENSG00000104059	FAM189A1	−1.616655842	0.048118333
ENSG00000158473	CD1D	−1.616742846	1.46245E−06
ENSG00000197859	ADAMTSL2	−1.619083779	5.69019E−07
ENSG00000154451	GBP5	−1.623010684	8.48054E−05
ENSG00000196358	NTNG2	−1.623642423	1.54908E−07
ENSG00000110848	CD69	−1.624764075	0.000777544
ENSG00000159650	UROC1	−1.625472907	0.006451973
ENSG00000185905	C16orf54	−1.626526294	7.89301E−07
ENSG00000102962	CCL22	−1.626752417	0.000659023
ENSG00000168334	XIRP1	−1.627111341	0.000254513
ENSG00000145649	GZMA	−1.628084686	0.000807992
ENSG00000167779	IGFBP6	−1.628820423	8.42388E−06
ENSG00000132704	FCRL2	−1.628822089	0.000176206
ENSG00000196159	FAT4	−1.629098699	2.11744E−07
ENSG00000198542	ITGBL1	−1.631791452	9.61473E−07
ENSG00000175857	GAPT	−1.631827958	3.37022E−07
ENSG00000124191	TOX2	−1.632292529	1.82257E−07
ENSG00000185274	WBSCR17	−1.632407931	5.51436E−06
ENSG00000167755	KLK6	−1.632699949	0.029537038

TABLE 3A-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000168490	PHYHIP	−1.634254375	3.86458E−07
ENSG00000197888	UGT2B17	−1.635503209	0.017174225
ENSG00000169031	COL4A3	−1.636189826	0.000137029
ENSG00000154258	ABCA9	−1.6368406	4.61249E−06
ENSG00000170801	HTRA3	−1.637259495	8.38017E−07
ENSG00000132840	BHMT2	−1.638443812	0.011133062
ENSG00000182326	C1S	−1.639428931	9.3156E−06
ENSG00000198821	CD247	−1.643666082	7.50175E−06
ENSG00000087258	GNAO1	−1.644143425	4.92172E−06
ENSG00000168477	TNXB	−1.645553842	4.79665E−07
ENSG00000185811	IKZF1	−1.647004425	1.20416E−07
ENSG00000169252	ADRB2	−1.650121928	4.73559E−06
ENSG00000140092	FBLN5	−1.651961926	4.92172E−06
ENSG00000183918	SH2D1A	−1.652848808	0.000221726
ENSG00000135298	BAI3	−1.653296552	1.45136E−05
ENSG00000182183	FAM159A	−1.655531231	8.90555E−06
ENSG00000175189	INHBC	−1.655769735	0.013044116
ENSG00000141338	ABCA8	−1.656965425	0.001659299
ENSG00000182902	SLC25A18	−1.65954025	0.039343824
ENSG00000219438	FAM19A5	−1.660585957	2.11475E−08
ENSG00000117594	HSD11B1	−1.661539712	0.000131636
ENSG00000107742	SPOCK2	−1.661835729	9.56676E−07
ENSG00000167757	KLK11	−1.662496263	0.001152839
ENSG00000101204	CHRNA4	−1.663842628	0.01603096
ENSG00000122224	LY9	−1.664420811	6.38526E−06
ENSG00000134193	REG4	−1.664764625	0.00455041
ENSG00000094963	FMO2	−1.666056541	2.47492E−06
ENSG00000123329	ARHGAP9	−1.666384228	3.7402E−08
ENSG00000109943	CRTAM	−1.66655714	1.14568E−05
ENSG00000177990	DPY19L2	−1.668198172	0.000278385
ENSG00000159231	CBR3	−1.66959019	6.18202E−06
ENSG00000163687	DNASE1L3	−1.669605674	0.007120277
ENSG00000160856	FCRL3	−1.671885886	0.001019428
ENSG00000104814	MAP4K1	−1.671903082	7.37367E−07
ENSG00000185669	SNAI3	−1.671932594	2.30806E−05
ENSG00000181143	MUC16	−1.674323132	0.018339127
ENSG00000149256	TENM4	−1.675077475	3.08739E−07
ENSG00000149534	MS4A2	−1.67656614	3.74637E−06
ENSG00000116824	CD2	−1.676720886	6.86303E−05
ENSG00000166428	PLD4	−1.677504294	6.62967E−07
ENSG00000124785	NRN1	−1.679063148	0.030891954
ENSG00000106333	PCOLCE	−1.681114376	3.86029E−10
ENSG00000163564	PYHIN1	−1.682661941	0.000669298
ENSG00000198846	TOX	−1.683762457	0.00012471
ENSG00000172236	TPSAB1	−1.685002747	3.24427E−05
ENSG00000100652	SLC10A1	−1.687961533	0.043142038
ENSG00000130005	GAMT	−1.688620091	0.002831199
ENSG00000118526	TCF21	−1.689694726	1.82257E−07
ENSG00000185479	KRT6B	−1.689922723	0.024466871
ENSG00000144218	AFF3	−1.694414456	2.44028E−06
ENSG00000187048	CYP4A11	−1.695406305	0.035374251
ENSG00000172497	ACOT12	−1.696164082	0.031654747
ENSG00000116106	EPHA4	−1.698555283	0.000147918
ENSG00000089012	SIRPG	−1.700868238	0.000153154
ENSG00000125148	MT2A	−1.701211079	5.66399E−05
ENSG00000013297	CLDN11	−1.702569289	7.30473E−08
ENSG00000117090	SLAMF1	−1.703205322	3.42517E−07
ENSG00000091831	ESR1	−1.705792155	2.62136E−06
ENSG00000157551	KCNJ15	−1.706433055	0.00011331
ENSG00000099994	SUSD2	−1.70688574	1.67438E−08
ENSG00000129009	ISLR	−1.70768258	8.30629E−08
ENSG00000042062	FAM65C	−1.709721194	0.000409868
ENSG00000271503	CCL5	−1.711093117	1.25536E−06
ENSG00000186265	BTLA	−1.711192354	7.89159E−05
ENSG00000009790	TRAF3IP3	−1.712431415	9.733E−08
ENSG00000140279	DUOX2	−1.718269856	0.001839583
ENSG00000153283	CD96	−1.722446739	4.2153E−05
ENSG00000145936	KCNMB1	−1.722680759	2.54675E−08
ENSG00000131196	NFATC1	−1.725169239	2.11475E−08
ENSG00000117643	MAN1Cl	−1.726462069	2.11475E−08
ENSG00000085265	FCN1	−1.72667995	3.16967E−06
ENSG00000154262	ABCA6	−1.726777063	2.38468E−06
ENSG00000170476	MZB1	−1.726853788	0.000127618
ENSG00000174307	PHLDA3	−1.72817549	3.14471E−07
ENSG00000139220	PPFIA2	−1.729023899	1.92084E−05

TABLE 3A-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000109758	HGFAC	−1.732231032	0.012227415
ENSG00000112175	BMP5	−1.732616549	0.000255946
ENSG00000106034	CPED1	−1.734018794	4.54336E−07
ENSG00000100351	GRAP2	−1.736449607	3.92415E−08
ENSG00000105664	COMP	−1.736599018	7.85645E−05
ENSG00000120907	ADRA1A	−1.738244194	0.045728705
ENSG00000263264	CTB-133G6.1	−1.740327674	0.000141667
ENSG00000167286	CD3D	−1.740381311	5.30868E−05
ENSG00000204866	IGFL2	−1.742775941	1.4293E−06
ENSG00000103522	IL21R	−1.74310075	1.16962E−06
ENSG00000105352	CEACAM4	−1.744678061	2.38468E−06
ENSG00000172349	IL16	−1.745060183	1.86227E−08
ENSG00000126231	PROZ	−1.747955437	0.016371477
ENSG00000197057	DTHD1	−1.749866928	0.000139515
ENSG00000139193	CD27	−1.751846546	2.10734E−05
ENSG00000025423	HSD17B6	−1.755989093	0.008558788
ENSG00000039537	C6	−1.757524211	0.04246576
ENSG00000170373	CST1	−1.757993922	0.036301707
ENSG00000163568	AIM2	−1.758409452	9.88776E−05
ENSG00000109684	CLNK	−1.760001006	8.55803E−06
ENSG00000099998	GGT5	−1.760531218	1.67438E−08
ENSG00000081052	COL4A4	−1.763469313	1.56991E−07
ENSG00000109906	ZBTB16	−1.763666181	0.002274733
ENSG00000164107	HAND2	−1.765677171	1.4631E−07
ENSG00000173040	EVC2	−1.76745187	1.89078E−09
ENSG00000147443	DOK2	−1.772561202	6.51487E−07
ENSG00000169715	MT1E	−1.775885047	0.000152182
ENSG00000196188	CTSE	−1.776727632	0.002499377
ENSG00000152969	JAKMIP1	−1.778936736	9.41953E−07
ENSG00000168229	PTGDR	−1.779594433	0.000508899
ENSG00000108381	ASPA	−1.784171677	6.28688E−05
ENSG00000135426	TESPA1	−1.784541597	3.75146E−06
ENSG00000064205	WISP2	−1.785179649	7.5572E−05
ENSG00000160593	AMICA1	−1.788120659	3.34865E−08
ENSG00000105509	HAS1	−1.789625772	3.86669E−05
ENSG00000050555	LAMC3	−1.791831208	8.02783E−05
ENSG00000106538	RARRES2	−1.792914945	7.89301E−07
ENSG00000218336	TENM3	−1.793825315	0.000330204
ENSG00000132465	IGJ	−1.794909121	0.000268589
ENSG00000144649	FAM198A	−1.795310856	5.71046E−05
ENSG00000110777	POU2AF1	−1.796428571	3.12173E−05
ENSG00000131459	GFPT2	−1.796743187	7.30473E−08
ENSG00000140368	PSTPIP1	−1.797172537	5.40421E−08
ENSG00000166250	CLMP	−1.799025045	4.64967E−05
ENSG00000167178	ISLR2	−1.80040134	2.28172E−07
ENSG00000174175	SELP	−1.800654289	6.65599E−06
ENSG00000156886	ITGAD	−1.805375882	1.36379E−05
ENSG00000134539	KLRD1	−1.813285483	1.95046E−06
ENSG00000159403	C1R	−1.813324895	2.07859E−06
ENSG00000151224	MAT1A	−1.816081848	0.043016212
ENSG00000110436	SLC1A2	−1.81621643	0.007372737
ENSG00000151892	GFRA1	−1.820928128	0.000809181
ENSG00000172346	CSDC2	−1.824103968	2.58144E−05
ENSG00000162365	CYP4A22	−1.825563247	0.019467695
ENSG00000090539	CHRD	−1.826733716	6.099E−06
ENSG00000180447	GAS1	−1.826917582	1.46245E−06
ENSG00000105122	RASAL3	−1.828017072	2.38902E−08
ENSG00000105989	WNT2	−1.836139896	3.64866E−08
ENSG00000205045	SLFN12L	−1.836470932	2.32958E−08
ENSG00000162493	PDPN	−1.836830676	7.23692E−06
ENSG00000163492	CCDC141	−1.83690351	1.52249E−05
ENSG00000171385	KCND3	−1.837334691	1.63415E−05
ENSG00000087245	MMP2	−1.839379635	2.027E−07
ENSG00000189233	NUGGC	−1.839733753	0.00180492
ENSG00000152495	CAMK4	−1.839956771	6.36692E−08
ENSG00000169851	PCDH7	−1.842391319	5.66683E−07
ENSG00000077984	CST7	−1.843553715	4.84108E−05
ENSG00000126353	CCR7	−1.845908873	0.000121606
ENSG00000091513	TF	−1.847238949	0.042339945
ENSG00000272636	DOC2B	−1.84776899	2.67007E−05
ENSG00000145423	SFRP2	−1.851133938	0.007875051
ENSG00000029534	ANK1	−1.852965994	7.07184E−08
ENSG00000152784	PRDM8	−1.856334997	8.2985E−08
ENSG00000127954	STEAP4	−1.8615322	1.13189E−05
ENSG00000011465	DCN	−1.862962082	9.9073E−08

TABLE 3A-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000144857	BOC	−1.865221827	5.92715E−08
ENSG00000122025	FLT3	−1.86617214	1.64174E−05
ENSG00000214402	LCNL1	−1.869824232	0.000138259
ENSG00000100346	CACNA1I	−1.869836037	0.000559201
ENSG00000156475	PPP2R2B	−1.870638406	7.91103E−07
ENSG00000113263	ITK	−1.876696984	3.00113E−06
ENSG00000163395	IGFN1	−1.880251791	0.000205549
ENSG00000189320	FAM180A	−1.881797326	1.69401E−06
ENSG00000152583	SPARCL1	−1.881878215	1.9548E−07
ENSG00000140285	FGF7	−1.884272369	0.000344444
ENSG00000205795	CYS1	−1.884441345	1.17091E−06
ENSG00000205784	ARRDC5	−1.899477613	1.05902E−06
ENSG00000172482	AGXT	−1.900227176	0.023398913
ENSG00000060709	RIMBP2	−1.901046353	0.00191795
ENSG00000175463	TBC1D10C	−1.90407368	4.79665E−07
ENSG00000250799	PRODH2	−1.910127685	0.007837018
ENSG00000153292	GPR110	−1.911516006	0.000392148
ENSG00000162552	WNT4	−1.912081822	6.55218E−08
ENSG00000182836	PLCXD3	−1.919350408	2.67007E−05
ENSG00000183778	B3GALT5	−1.921511887	5.4965E−06
ENSG00000125384	PTGER2	−1.926307882	7.11386E−08
ENSG00000198851	CD3E	−1.926834494	1.9412E−07
ENSG00000205364	MT1M	−1.93278971	0.001076927
ENSG00000068831	RASGRP2	−1.934148078	9.47397E−08
ENSG00000149451	ADAM33	−1.939863642	1.52496E−05
ENSG00000173705	SUSD5	−1.941554039	1.68078E−05
ENSG00000172673	THEMIS	−1.942331165	5.9626E−07
ENSG00000168685	IL7R	−1.944567611	1.80121E−05
ENSG00000113088	GZMK	−1.95209464	5.62555E−05
ENSG00000161031	PGLYRP2	−1.957638292	0.027182082
ENSG00000180828	BHLHE22	−1.961742811	2.93627E−06
ENSG00000167984	NLRC3	−1.968699444	2.3508E−08
ENSG00000079931	MOXD1	−1.970809581	2.3508E−08
ENSG00000073861	TBX21	−1.972710767	3.64223E−05
ENSG00000072818	ACAP1	−1.973493751	3.64866E−08
ENSG00000163508	EOMES	−1.975206409	2.18735E−06
ENSG00000071991	CDH19	−1.976525894	6.92606E−06
ENSG00000275063	AC233755.1	−1.980211896	0.001328112
ENSG00000183160	TMEM119	−1.98856722	3.9501E−06
ENSG00000197253	TPSB2	−1.989161318	1.67571E−05
ENSG00000135144	DTX1	−1.989482455	4.0212E−05
ENSG00000137265	IRF4	−1.991133162	3.58567E−07
ENSG00000121410	A1BG	−1.994194759	2.39205E−05
ENSG00000244734	HBB	−1.996693638	1.82887E−06
ENSG00000134538	SLCO1B1	−1.997247617	0.024258756
ENSG00000140505	CYP1A2	−1.998480963	0.007359436
ENSG00000145934	TENM2	−2.005163875	2.88302E−05
ENSG00000115085	ZAP70	−2.008362263	3.43678E−07
ENSG00000188389	PDCD1	−2.013304666	1.0855E−05
ENSG00000110900	TSPAN11	−2.013727616	2.99849E−05
ENSG00000144908	ALDH1L1	−2.02257893	0.007027914
ENSG00000136011	STAB2	−2.023675331	0.001918481
ENSG00000160185	UBASH3A	−2.024512063	1.6877E−06
ENSG00000166482	MFAP4	−2.032069985	3.36232E−06
ENSG00000123453	SARDH	−2.036085745	1.17091E−06
ENSG00000047617	ANO2	−2.042553124	4.10994E−07
ENSG00000171812	COL8A2	−2.043031965	1.89078E−09
ENSG00000198650	TAT	−2.049538974	0.039892923
ENSG00000122787	AKR1D1	−2.050473152	0.002259074
ENSG00000177272	KCNA3	−2.059440975	2.64354E−08
ENSG00000140107	SLC25A47	−2.074759218	0.016748536
ENSG00000155657	TTN	−2.077272513	1.73385E−07
ENSG00000172061	LRRC15	−2.088920797	3.29885E−06
ENSG00000215644	GCGR	−2.094491352	0.00455041
ENSG00000147138	GPR174	−2.098204569	2.87088E−06
ENSG00000117601	SERPINC1	−2.101960398	0.046802435
ENSG00000169035	KLK7	−2.119202838	0.001130698
ENSG00000101188	NTSR1	−2.136271515	0.001365223
ENSG00000184956	MUC6	−2.142966072	0.007582781
ENSG00000138135	CH25H	−2.143580695	0.000289829
ENSG00000105697	HAMP	−2.147268816	0.000790785
ENSG00000129596	CDO1	−2.152713049	0.004311464
ENSG00000003137	CYP26B1	−2.154130063	1.65513E−06
ENSG00000132514	CLEC10A	−2.164002441	6.18202E−06
ENSG00000145692	BHMT	−2.172393141	0.022336562
ENSG00000121807	CCR2	−2.17920285	3.94158E−07
ENSG00000174946	GPR171	−2.180670676	8.19986E−05
ENSG00000163519	TRAT1	−2.183040612	2.15639E−05
ENSG00000154529	CNTNAP3B	−2.19207145	3.03667E−05
ENSG00000173578	XCR1	−2.197511235	1.28433E−05
ENSG00000143196	DPT	−2.200975281	4.61599E−06
ENSG00000119714	GPR68	−2.200996178	1.67438E−08
ENSG00000254709	IGLL5	−2.201894109	5.90052E−06
ENSG00000123500	COL10A1	−2.203898449	1.4631E−07
ENSG00000131386	GALNT15	−2.21041109	2.11475E−08
ENSG00000110799	VWF	−2.217632153	5.88447E−09
ENSG00000140835	CHST4	−2.248832453	0.000211595
ENSG00000110243	APOA5	−2.249011197	0.021109571
ENSG00000187634	SAMD11	−2.268098478	1.86227E−08
ENSG00000110245	APOC3	−2.279400193	0.044167829
ENSG00000118137	APOA1	−2.292998066	0.029453145
ENSG00000206384	COL6A6	−2.337054387	8.75035E−08
ENSG00000137077	CCL21	−2.339382377	1.8088E−05
ENSG00000166148	AVPR1A	−2.347452419	0.001434051
ENSG00000130649	CYP2E1	−2.365713616	0.001806626
ENSG00000255974	CYP2A6	−2.366850771	0.029623804
ENSG00000124203	ZNF831	−2.384341125	7.11386E−08
ENSG00000129451	KLK10	−2.423477225	0.00019224
ENSG00000196616	ADH1B	−2.436635188	0.005517265
ENSG00000140538	NTRK3	−2.441826477	5.0103E−08
ENSG00000156738	MS4A1	−2.503377804	8.38017E−07
ENSG00000136573	BLK	−2.521099289	3.35863E−06
ENSG00000136546	SCN7A	−2.534193956	1.35959E−05
ENSG00000107317	PTGDS	−2.567982401	3.42653E−08
ENSG00000172543	CTSW	−2.601624003	2.62703E−08
ENSG00000112936	C7	−2.734427236	6.99257E−06
ENSG00000172724	CCL19	−3.10276147	1.78025E−06

TABLE 3B

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000118137	APOA1	4.03342127	0.00020128
ENSG00000110245	APOC3	3.817494407	0.000895708
ENSG00000172482	AGXT	3.649556969	3.19938E−05
ENSG00000110243	APOA5	3.555420548	0.000365209
ENSG00000101204	CHRNA4	3.521926862	2.38615E−06
ENSG00000255974	CYP2A6	3.400280295	0.002039671
ENSG00000137204	SLC22A7	3.344034575	0.000526078
ENSG00000055957	ITIH1	3.318666831	0.000632477
ENSG00000215644	GCGR	3.313633037	2.0805E−05
ENSG00000140107	SLC25A47	3.214504508	0.000308981
ENSG00000145192	AHSG	3.201706797	0.002890618
ENSG00000140505	CYP1A2	3.164111782	5.71982E−05
ENSG00000163631	ALB	3.157004897	0.002452464
ENSG00000141485	SLC13A5	3.153757229	0.000102754
ENSG00000117601	SERPINC1	3.13709961	0.003306975
ENSG00000122194	PLG	3.12327998	0.004005088
ENSG00000161031	PGLYRP2	3.097960789	0.000606349
ENSG00000158104	HPD	3.095102273	0.001768852
ENSG00000228278	ORM2	3.091738751	0.001237175
ENSG00000173432	SAA1	3.091244007	0.001422055
ENSG00000156222	SLC28A1	3.074992314	1.67555E−05
ENSG00000109758	HGFAC	3.045511033	2.85412E−05
ENSG00000120907	ADRA1A	3.037827378	0.000607279
ENSG00000257017	HP	3.037527154	0.01404727
ENSG00000198650	TAT	3.008538872	0.002902688
ENSG00000130649	CYP2E1	2.981681371	0.000162521
ENSG00000105707	HPN	2.981679795	6.19929E−05
ENSG00000172724	CCL19	2.963589155	5.23278E−06
ENSG00000145692	BHMT	2.940080806	0.002326865
ENSG00000159650	UROC1	2.931689347	4.46195E−06
ENSG00000105398	SULT2A1	2.895943776	0.001125162
ENSG00000161944	ASGR2	2.886375795	0.000244032
ENSG00000073754	CD5L	2.884937538	0.000185574
ENSG00000175189	INHBC	2.879896728	3.97202E−05
ENSG00000157131	C8A	2.871228568	0.006196416

TABLE 3B-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000147647	DPYS	2.861699945	0.000605481
ENSG00000151224	MAT1A	2.853444253	0.001735388
ENSG00000118271	TTR	2.852019202	0.007471748
ENSG00000122787	AKR1D1	2.851571077	4.68552E−05
ENSG00000079557	AFM	2.847947396	0.004612123
ENSG00000009724	MASP2	2.840850223	0.000860058
ENSG00000126231	PROZ	2.815787191	0.000192046
ENSG00000109072	VTN	2.805293077	0.001565125
ENSG00000178772	CPN2	2.801411839	0.001099451
ENSG00000250799	PRODH2	2.80028653	0.000173312
ENSG00000187048	CYP4A11	2.796840372	0.000719964
ENSG00000162365	CYP4A22	2.782937306	0.000532431
ENSG00000160282	FTCD	2.765798702	0.000559263
ENSG00000131187	F12	2.755837253	1.92409E−07
ENSG00000158874	APOA2	2.755273623	0.013072978
ENSG00000100652	SLC10A1	2.749245822	0.001183352
ENSG00000196600	SLC22A25	2.73014871	0.000628883
ENSG00000066813	ACSM2B	2.726292317	0.001969372
ENSG00000105697	HAMP	2.712303827	4.53987E−05
ENSG00000113905	HRG	2.70641239	0.015993876
ENSG00000106927	AMBP	2.704162113	0.006237735
ENSG00000180210	F2	2.699176393	0.002605332
ENSG00000171560	FGA	2.693980117	0.00255617
ENSG00000139269	INHBE	2.688059199	0.000230634
ENSG00000131482	G6PC	2.684880323	0.003603728
ENSG00000166148	AVPR1A	2.670331491	0.000408681
ENSG00000187758	ADH1A	2.666188722	0.008182502
ENSG00000182902	SLC25A18	2.649043378	0.001183394
ENSG00000180432	CYP8B1	2.643870861	0.004220946
ENSG00000138207	RBP4	2.63884479	0.002229992
ENSG00000101323	HAO1	2.63869104	0.001750212
ENSG00000244731	C4A	2.638540175	9.85035E−06
ENSG00000162267	ITIH3	2.616213914	0.001394604
ENSG00000156738	MS4A1	2.614889948	4.72612E−07
ENSG00000091513	TF	2.599465774	0.004936377
ENSG00000186910	SERPINA11	2.586296044	0.005890983
ENSG00000181790	BAI1	2.568319627	1.87301E−08
ENSG00000168509	HFE2	2.565607791	0.001891022
ENSG00000189233	NUGGC	2.542269974	3.59335E−05
ENSG00000141505	ASGR1	2.54217327	0.000163093
ENSG00000106327	TFR2	2.541081148	7.88371E−05
ENSG00000167711	SERPINF2	2.536203015	4.71562E−05
ENSG00000167588	GPD1	2.516540158	2.10921E−06
ENSG00000134389	CFHR5	2.51553596	0.003266532
ENSG00000163687	DNASE1L3	2.51349642	9.92817E−05
ENSG00000099769	IGFALS	2.511431301	2.84079E−05
ENSG00000060566	CREB3L3	2.51092543	0.00037388
ENSG00000183747	ACSM2A	2.499331636	0.001401275
ENSG00000138109	CYP2C9	2.496237434	0.002477368
ENSG00000167676	PLIN4	2.484747629	0.000100961
ENSG00000163581	SLC2A2	2.474354607	0.016215986
ENSG00000125144	MT1G	2.467085048	2.71347E−05
ENSG00000142748	FCN3	2.464592475	5.11234E−05
ENSG00000172497	ACOT12	2.460074753	0.002117129
ENSG00000244414	CFHR1	2.455634101	0.006590488
ENSG00000021852	C8B	2.452331363	0.009125228
ENSG00000184956	MUC6	2.448967667	0.002600485
ENSG00000166183	ASPG	2.441975552	1.07579E−05
ENSG00000134339	SAA2	2.436739409	0.002929755
ENSG00000118520	ARG1	2.431413131	0.004864395
ENSG00000214456	PLIN5	2.411934168	2.15966E−05
ENSG00000146678	IGFBP1	2.400626989	0.005979301
ENSG00000088926	F11	2.392702358	0.008411284
ENSG00000084674	APOB	2.380551386	0.011620388
ENSG00000139547	RDH16	2.378004222	7.0753E−05
ENSG00000157087	ATP2B2	2.368883131	0.002117311
ENSG00000113889	KNG1	2.367626386	0.018695719
ENSG00000130173	C190rf80	2.364577006	0.004209745
ENSG00000171236	LRG1	2.36171303	6.87212E−06
ENSG00000129988	LBP	2.359732338	0.005841357
ENSG00000025423	HSD17B6	2.359462566	0.000634618
ENSG00000113600	C9	2.330342283	0.027453219
ENSG00000182327	GLTPD2	2.326087705	3.50261E−05
ENSG00000091583	APOH	2.324805638	0.047565572
ENSG00000198099	ADH4	2.314677646	0.017707948
ENSG00000130005	GAMT	2.313115142	8.2458E−05
ENSG00000145850	TIMD4	2.311992794	0.00014789
ENSG00000039537	C6	2.311294572	0.008045726
ENSG00000116785	CFHR3	2.2878727	0.008480607
ENSG00000162551	ALPL	2.280386871	5.46105E−06
ENSG00000143627	PKLR	2.272664786	0.000602546
ENSG00000261701	HPR	2.272424321	0.01420778
ENSG00000229314	ORM1	2.26704992	0.025128422
ENSG00000084734	GCKR	2.266094526	0.000587665
ENSG00000143257	NR1I3	2.264813532	0.003087031
ENSG00000175336	APOF	2.264376716	0.008749459
ENSG00000198670	LPA	2.241502788	0.001099601
ENSG00000277893	SRD5A2	2.24024151	0.000766218
ENSG00000144908	ALDH1L1	2.239002548	0.003371363
ENSG00000187045	TMPRSS6	2.232259824	0.000121488
ENSG00000107317	PTGDS	2.22816392	7.1707E−07
ENSG00000101981	F9	2.227038159	0.02450203
ENSG00000124203	ZNF831	2.21137554	4.2107E−07
ENSG00000110887	DAO	2.210982589	0.000458996
ENSG00000174990	CA5A	2.206853287	0.000184293
ENSG00000136872	ALDOB	2.20497856	0.005457894
ENSG00000145626	UGT3A1	2.204846842	0.004959351
ENSG00000110169	HPX	2.198953128	0.002946105
ENSG00000160868	CYP3A4	2.188304321	0.025404392
ENSG00000103449	SALL1	2.187835144	0.000884892
ENSG00000125730	C3	2.184242808	0.000424251
ENSG00000197444	OGDHL	2.183148343	0.000652796
ENSG00000090539	CHRD	2.177775965	3.46838E−07
ENSG00000145321	GC	2.17078114	0.043649274
ENSG00000172543	CTSW	2.166094783	1.22945E−06
ENSG00000129596	CDO1	2.157586834	0.004892539
ENSG00000138315	OIT3	2.154636981	0.000348535
ENSG00000121410	A1BG	2.154024269	9.12813E−06
ENSG00000136011	STAB2	2.153895927	0.001170482
ENSG00000112337	SLC17A2	2.151273679	0.002490273
ENSG00000143921	ABCG8	2.140849758	0.006281255
ENSG00000120054	CPN1	2.140412287	0.008337442
ENSG00000163884	KLF15	2.136804934	0.000176568
ENSG00000196616	ADH1B	2.120909383	0.017166589
ENSG00000136573	BLK	2.120259343	7.79626E−05
ENSG00000188257	PLA2G2A	2.11905233	0.01547861
ENSG00000105374	NKG7	2.109664434	1.43089E−05
ENSG00000161896	IP6K3	2.106714009	0.001809755
ENSG00000073734	ABCB11	2.09464907	0.006671003
ENSG00000145708	CRHBP	2.080523576	0.003098848
ENSG00000169136	ATF5	2.074975467	3.34382E−08
ENSG00000170956	CEACAM3	2.071071455	6.53981E−06
ENSG00000162896	PIGR	2.067595291	0.037879176
ENSG00000138115	CYP2C8	2.062714257	0.030384223
ENSG00000177238	TRIM72	2.06137635	0.000541229
ENSG00000100024	UPB1	2.056548897	0.000887421
ENSG00000132840	BHMT2	2.056293226	0.001897798
ENSG00000100344	PNPLA3	2.055811223	0.000831964
ENSG00000111249	CUX2	2.052733446	0.000470832
ENSG00000120885	CLU	2.051071157	0.000430434
ENSG00000123453	SARDH	2.043937302	1.45867E−06
ENSG00000171564	FGB	2.038597238	0.044898114
ENSG00000168229	PTGDR	2.037806451	0.000134693
ENSG00000151948	GLT1D1	2.036591898	3.40188E−05
ENSG00000263264	CTB-133G6.1	2.032222551	1.84836E−05
ENSG00000183549	ACSM5	2.031757331	0.000901791
ENSG00000162897	FCAMR	2.02756664	4.90232E−06
ENSG00000188389	PDCD1	2.022802834	1.33473E−05
ENSG00000171798	KNDC1	2.01574676	0.004354954
ENSG00000151892	GFRA1	2.011732065	0.000368787
ENSG00000149527	PLCH2	2.008865677	4.66585E−08
ENSG00000176919	C8G	2.007593899	0.000165191
ENSG00000104760	FGL1	2.007114479	0.035150116
ENSG00000113492	AGXT2	2.005682188	0.008337442
ENSG00000115718	PROC	2.005098773	0.000808643
ENSG00000072818	ACAP1	2.003565112	2.83645E−08
ENSG00000165471	MBL2	1.99513021	0.020127504
ENSG00000090534	THPO	1.994330177	2.76651E−05
ENSG00000146147	MLIP	1.991597761	0.003784608
ENSG00000099937	SERPIND1	1.98233912	0.0305223

TABLE 3B-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000243696	RPS-966M1.6	1.978888481	0.000292106
ENSG00000132703	APCS	1.976538082	0.0252356
ENSG00000224389	C4B	1.975395043	0.000960287
ENSG00000132514	CLEC10A	1.964789409	4.44362E−05
ENSG00000021826	CPS1	1.963326101	0.028428885
ENSG00000135144	DTX1	1.958723636	6.69335E−05
ENSG00000005421	PON1	1.957557669	0.007436136
ENSG00000130222	GADD45G	1.953456897	4.3641E−07
ENSG00000136574	GATA4	1.9515903	2.0805E−05
ENSG00000275152	CCL16	1.94269905	0.00406139
ENSG00000132693	CRP	1.940142174	0.026905704
ENSG00000122679	RAMP3	1.939738533	3.46324E−08
ENSG00000138798	EGF	1.938228743	0.011819496
ENSG00000159261	CLDN14	1.928305056	6.01076E−05
ENSG00000178297	TMPRSS9	1.927239153	0.000121913
ENSG00000100346	CACNA1I	1.919037239	0.000515575
ENSG00000073861	TBX21	1.918366563	7.86285E−05
ENSG00000124721	DNAH8	1.913703166	0.003148436
ENSG00000138356	AOX1	1.9118762	0.015369331
ENSG00000187193	MT1X	1.910199557	0.000396357
ENSG00000140835	CHST4	1.910062582	0.001748491
ENSG00000105122	RASAL3	1.897616857	1.18923E−08
ENSG00000196990	FAM163B	1.896368518	6.23831E−05
ENSG00000138075	ABCG5	1.8908586	0.008784112
ENSG00000131910	NR0B2	1.882096536	6.71783E−05
ENSG00000103313	MEFV	1.879687195	1.87175E−06
ENSG00000093134	VNN3	1.876205783	0.00020497
ENSG00000125735	TNFSF14	1.875354108	7.64183E−05
ENSG00000129451	KLK10	1.873471736	0.003739833
ENSG00000003137	CYP26B1	1.870052122	2.68514E−05
ENSG00000111713	GYS2	1.869332676	0.022629452
ENSG00000101188	NTSR1	1.868718916	0.00664869
ENSG00000177989	ODF3B	1.866218494	2.01349E−09
ENSG00000110799	VWF	1.865960751	1.98697E−07
ENSG00000111181	SLC6Al2	1.863396594	7.39367E−06
ENSG00000187634	SAMD11	1.863359824	9.81754E−07
ENSG00000123561	SERPINA7	1.863050591	0.011816054
ENSG00000154529	CNTNAP3B	1.862816347	0.000420871
ENSG00000116882	HAO2	1.861459243	0.010122264
ENSG00000170099	SERPINA6	1.861176824	0.017215754
ENSG00000173762	CD7	1.859863899	4.91527E−05
ENSG00000175463	TBC1D10C	1.857724152	9.81643E−07
ENSG00000275395	FCGBP	1.856369357	0.000393254
ENSG00000115085	ZAP70	1.852736123	2.24704E−06
ENSG00000064205	WISP2	1.848100926	8.29329E−05
ENSG00000109181	UGT2B10	1.84802304	0.007673297
ENSG00000130203	APOE	1.847688106	2.41717E−06
ENSG00000104814	MAP4K1	1.845552821	1.35732E−07
ENSG00000147573	TRIM55	1.844837192	0.001479829
ENSG00000168874	ATOH8	1.842839027	0.003377482
ENSG00000115523	GNLY	1.838744124	7.3608E−05
ENSG00000167483	FAM129C	1.838608685	0.000170872
ENSG00000153086	ACMSD	1.836524586	0.008566197
ENSG00000100197	CYP2D6	1.829953247	3.18759E−05
ENSG00000152969	JAKMIP1	1.825972754	9.78322E−07
ENSG00000231852	CYP21A2	1.823917763	0.000903462
ENSG00000140279	DUOX2	1.823491986	0.001415904
ENSG00000100665	SERPINA4	1.82299406	0.016959498
ENSG00000042062	FAM65C	1.822157789	0.000235797
ENSG00000234906	APOC2	1.821542303	0.000209567
ENSG00000214402	LCNL1	1.820340091	0.000265435
ENSG00000205358	MT1H	1.810540297	0.006501419
ENSG00000062524	LTK	1.80931079	0.000121085
ENSG00000169715	MT1E	1.808512373	0.000180499
ENSG00000136457	CHAD	1.804802571	0.001625712
ENSG00000126353	CCR7	1.803144527	0.000218428
ENSG00000205364	MT1M	1.801744376	0.002967506
ENSG00000139194	RBP5	1.801713544	0.000565551
ENSG00000182156	ENPP7	1.801390039	0.000822806
ENSG00000126759	CFP	1.800923596	4.41807E−08
ENSG00000167476	JSRP1	1.79911915	2.44145E−06
ENSG00000083807	SLC27A5	1.798153138	2.76661E−05
ENSG00000145934	TENM2	1.796457258	0.000206303
ENSG00000110665	C11orf21	1.794329286	0.000202608
ENSG00000188282	RUFY4	1.79268797	0.000135845

TABLE 3B-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000188488	SERPINA5	1.792614048	0.009784986
ENSG00000243955	GSTA1	1.792056651	0.039652316
ENSG00000129993	CBFA2T3	1.791485388	1.4732E−07
ENSG00000186891	TNFRSF18	1.789424486	3.96031E−06
ENSG00000085265	FCN1	1.786385951	3.02782E−06
ENSG00000084110	HAL	1.786196272	0.002407662
ENSG00000183971	NPW	1.784741632	5.98994E−05
ENSG00000180875	GREM2	1.783092041	0.004913974
ENSG00000171385	KCND3	1.783042994	3.94309E−05
ENSG00000105352	CEACAM4	1.777033354	2.74807E−06
ENSG00000156234	CXCL13	1.773676728	0.006035938
ENSG00000158517	NCF1	1.77360529	5.40951E−06
ENSG00000008516	MMP25	1.770426818	1.41769E−08
ENSG00000073150	PANX2	1.767576887	6.59553E−05
ENSG00000068831	RASGRP2	1.764610407	8.61631E−07
ENSG00000173531	MST1	1.762894187	5.3942E−06
ENSG00000167984	NLRC3	1.762572294	2.60598E−07
ENSG00000065320	NTN1	1.759391095	0.000799961
ENSG00000244734	HBB	1.757053542	3.25222E−05
ENSG00000124713	GNMT	1.755868292	2.97612E−05
ENSG00000162460	TMEM82	1.754068694	0.002354755
ENSG00000175003	SLC22A1	1.752026696	0.000997327
ENSG00000183837	PNMA3	1.749215247	0.000301841
ENSG00000197249	SERPINA1	1.748262514	0.004605234
ENSG00000123838	C4BPA	1.746288822	0.028529213
ENSG00000153404	PLEKHG4B	1.745974706	0.000654856
ENSG00000157168	NRG1	1.74589881	0.003843138
ENSG00000089692	LAG3	1.74502125	4.73742E−07
ENSG00000105369	CD79A	1.741335371	5.69744E−05
ENSG00000180155	LYNX1	1.738389995	8.02263E−06
ENSG00000104899	AMH	1.738354537	2.66697E−05
ENSG00000170476	MZB1	1.734569723	0.000194664
ENSG00000128011	LRFN1	1.732331141	6.28875E−05
ENSG00000125148	MT2A	1.730950364	7.13542E−05
ENSG00000275063	AC233755.1	1.729322212	0.006172039
ENSG00000055955	ITIH4	1.728177973	0.001930577
ENSG00000106538	RARRES2	1.726013818	2.76745E−06
ENSG00000156096	UGT2B4	1.725495377	0.043548679
ENSG00000146054	TRIM7	1.72495903	0.000205372
ENSG00000160856	FCRL3	1.722631911	0.000936308
ENSG00000005471	ABCB4	1.719080718	0.002526075
ENSG00000172955	ADH6	1.716421501	0.020567262
ENSG00000167874	TMEM88	1.715010922	0.000109369
ENSG00000054938	CHRDL2	1.713564832	0.001977651
ENSG00000088827	SIGLEC1	1.711830538	3.12674E−05
ENSG00000227507	LTB	1.708765213	1.53852E−05
ENSG00000204632	HLA-G	1.70456412	0.000110853
ENSG00000131203	IDO1	1.703930695	0.006901392
ENSG00000137077	CCL21	1.701411468	0.001644306
ENSG00000254521	SIGLEC12	1.698716313	9.94122E−05
ENSG00000163959	SLC51A	1.698224278	0.00247345
ENSG00000177272	KCNA3	1.697480235	1.94598E−06
ENSG00000139800	ZIC5	1.689500353	0.005955401
ENSG00000104059	FAM189A1	1.685372264	0.041153881
ENSG00000159423	ALDH4A1	1.685164073	1.09581E−05
ENSG00000120949	TNFRSF8	1.67495086	7.49844E−06
ENSG00000117215	PLA2G2D	1.674749325	0.010529388
ENSG00000248144	ADH1C	1.669403836	0.04953767
ENSG00000180767	CHST13	1.66820775	0.004391163
ENSG00000182183	FAM159A	1.666525444	1.41849E−05
ENSG00000181444	ZNF467	1.666197793	1.66452E−07
ENSG00000140961	OSGIN1	1.665643214	9.24674E−08
ENSG00000187608	ISG15	1.662520176	0.001746152
ENSG00000110436	SLC1A2	1.659988783	0.016249596
ENSG00000206384	COL6A6	1.653792903	0.000117908
ENSG00000165125	TRPV6	1.652612132	0.00368298
ENSG00000225968	ELFN1	1.651208878	1.47141E−06
ENSG00000254788	CKLF-CMTM1	1.64958526	9.08287E−07
ENSG00000057593	F7	1.647953549	0.024882783
ENSG00000168477	TNXB	1.646578783	7.81703E−07
ENSG00000138823	MTTP	1.6461343	0.016189652
ENSG00000189410	SH2D5	1.643968913	0.002705987
ENSG00000166823	MESP1	1.642477892	0.000445012
ENSG00000185338	SOCS1	1.639791845	6.65962E−07
ENSG00000140368	PSTPIP1	1.637320915	4.81596E−07

TABLE 3B-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000015520	NPC1L1	1.635491238	0.001045583
ENSG00000167772	ANGPTL4	1.634398094	1.98855E−05
ENSG00000131386	GALNT15	1.633087575	9.47614E−06
ENSG00000166106	ADAMTS15	1.632711035	0.00114866
ENSG00000109906	ZBTB16	1.629223454	0.0061776
ENSG00000116690	PRG4	1.628432381	0.007704889
ENSG00000134571	MYBPC3	1.628364503	3.18019E−05
ENSG00000132704	FCRL2	1.627384887	0.000283186
ENSG00000173578	XCR1	1.626175318	0.001112116
ENSG00000147443	DOK2	1.621123096	4.19841E−06
ENSG00000161653	NAGS	1.62093036	6.88702E−07
ENSG00000168546	GFRA2	1.618891903	0.002653066
ENSG00000123843	C4BPB	1.615265955	6.72693E−05
ENSG00000185499	MUC1	1.614882918	0.003146832
ENSG00000089012	SIRPG	1.614629752	0.000410911
ENSG00000180644	PRF1	1.60984838	0.000353497
ENSG00000130487	KLHDC7B	1.609401829	2.95717E−06
ENSG00000130812	ANGPTL6	1.609247334	0.000203163
ENSG00000271503	CCL5	1.608717196	6.72864E−06
ENSG00000174326	SLC16A11	1.603389799	0.000400232
EN5G00000164850	GPER1	1.602617044	0.000628996
ENSG00000198417	MT1F	1.602377217	8.1754E−06
EN5G00000280789	PAGR1	1.602104346	3.03492E−06
EN5G00000129946	SHC2	1.600778342	2.53183E−07
ENSG00000141574	SECTM1	1.598597388	1.16026E−05
ENSG00000140274	DUOXA2	1.597244432	0.006036338
ENSG00000124256	ZBP1	1.593895754	5.12655E−05
ENSG00000176720	BOK	1.59208335	1.61964E−08
ENSG00000180096	SEPT1	1.590954812	6.12664E−07
ENSG00000171234	UGT2B7	1.588703972	0.004784474
ENSG00000133246	PRAM1	1.588436941	1.65774E−08
ENSG00000007908	SELE	1.587950519	0.004511819
ENSG00000096996	IL12RB1	1.585877225	5.33991E−07
ENSG00000136490	LIMD2	1.585202182	9.87742E−08
ENSG00000166035	LIPC	1.585189629	0.004337306
ENSG00000115226	FNDC4	1.584730002	2.62044E−05
ENSG00000163508	EOMES	1.584296602	0.000129922
ENSG00000198610	AKR1C4	1.582907202	0.0223585
ENSG00000167680	SEMA6B	1.581726298	2.56029E−09
ENSG00000118804	FAM47E−STBD1	1.581707821	6.61276E−07
ENSG00000092607	TBX15	1.581137159	0.002725107
ENSG00000188536	HBA2	1.580952966	0.000145343
ENSG00000258472	RP11-192H23.4	1.580107392	4.78837E−08
ENSG00000203883	SOX18	1.579196193	9.0363E−09
ENSG00000105609	LILRB5	1.579144678	0.002356928
ENSG00000099377	HSD3B7	1.578351001	2.01349E−09
ENSG00000187260	WDR86	1.578246045	2.72846E−06
ENSG00000139193	CD27	1.576787928	0.000167422
ENSG00000108950	FAM20A	1.569323478	5.89966E−05
ENSG00000142512	SIGLEC10	1.558451603	1.16876E−06
ENSG00000186994	KANK3	1.558328138	1.61808E−07
ENSG00000134363	FST	1.558053549	0.012573902
ENSG00000179348	GATA2	1.556181299	6.31175E−06
ENSG00000064201	TSPAN32	1.556158659	0.004222363
ENSG00000186642	PDE2A	1.555302924	8.08213E−06
ENSG00000143196	DPT	1.55438042	0.001172053
ENSG00000104972	LILRB1	1.552571458	3.1956E−07
ENSG00000107147	KCNT1	1.550415416	0.023504834
ENSG00000184979	USP18	1.548316322	2.28753E−05
ENSG00000122223	CD244	1.545519949	0.00024182
ENSG00000158445	KCNB1	1.544809945	0.013214337
ENSG00000160185	UBASH3A	1.53615082	0.000194244
ENSG00000102879	CORO1A	1.53399304	4.94145E−07
ENSG00000185739	SRL	1.532845494	0.000197044
ENSG00000204642	HLA-F	1.532253799	9.84429E−06
ENSG00000180871	CXCR2	1.531703143	2.47874E−05
ENSG00000169083	AR	1.531236164	0.002033423
ENSG00000187116	LILRA5	1.531201843	0.000166288
ENSG00000146192	FGD2	1.530806368	3.709E−08
ENSG00000025708	TYMP	1.526764551	6.36576E−07
ENSG00000170458	CD14	1.523186839	1.22091E−05
ENSG00000182853	VMO1	1.520279287	0.000413367
ENSG00000145217	SLC26A1	1.519696327	5.34812E−05
ENSG00000162676	GFI1	1.519455566	9.85814E−06
ENSG00000130270	ATP8B3	1.51752289	8.04517E−06
ENSG00000204099	NEU4	1.514399269	0.000284209
ENSG00000166825	ANPEP	1.514176695	0.000156096
ENSG00000104974	LILRA1	1.513547989	3.66484E−05
ENSG00000135094	SDS	1.512678166	0.000420758
ENSG00000159761	C16orf86	1.511460887	1.41334E−05
ENSG00000197558	SSPO	1.51104646	4.27128E−05
ENSG00000124191	TOX2	1.510051746	1.65239E−06
ENSG00000009694	TENM1	1.50553148	0.010618274
ENSG00000272636	DOC2B	1.501787011	0.000706486
ENSG00000160883	HK3	1.501399726	2.90159E−06
ENSG00000136305	CIDEB	1.501381456	4.48948E−06
ENSG00000113088	GZMK	1.500758813	0.002084863
ENSG00000167992	VWCE	1.49937759	0.003394657
ENSG00000103522	IL21R	1.497217502	2.3103E−05
ENSG00000130208	APOC1	1.496848549	0.003538667
ENSG00000180509	KCNE1	1.493422865	0.000223845
ENSG00000185669	SNAI3	1.490036928	0.000170417
ENSG00000107159	CA9	1.48921772	0.012780816
ENSG00000243649	CFB	1.48806145	0.000145343
ENSG00000188305	C19orf35	1.487580548	7.42914E−05
ENSG00000160801	PTH1R	1.487389486	0.001178722
ENSG00000196090	PTPRT	1.486605225	0.001355525
ENSG00000188517	COL25A1	1.485873647	0.001531804
ENSG00000254709	IGLL5	1.485808498	0.001990999
ENSG00000134962	KLB	1.48180961	0.005137395
ENSG00000159307	SCUBE1	1.481616838	0.000256796
ENSG00000107742	SPOCK2	1.480342214	1.13584E−05
ENSG00000162747	FCGR3B	1.479926439	0.000394616
ENSG00000184557	SOCS3	1.479596519	6.52137E−06
ENSG00000173599	PC	1.479467656	1.49065E−05
ENSG00000244474	UGT1A4	1.479087428	0.032746482
ENSG00000187889	C1orf168	1.47363403	0.008517697
ENSG00000105509	HAS1	1.473448956	0.000911515
ENSG00000182885	GPR97	1.472956397	7.99165E−05
ENSG00000150656	CNDP1	1.472736717	0.004443654
ENSG00000160932	LY6E	1.470833109	3.50003E−06
ENSG00000115457	IGFBP2	1.468493667	0.002859981
ENSG00000158473	CD1D	1.465852202	1.49296E−05
ENSG00000127220	ABHD8	1.463150875	7.6543E−06
ENSG00000074660	SCARF1	1.463099519	6.50364E−10
ENSG00000162572	SCNN1D	1.461799829	3.78361E−06
ENSG00000156127	BATF	1.460660543	1.01302E−05
ENSG00000135447	PPP1R1A	1.459770857	0.042126222
ENSG00000105246	EBI3	1.458884775	0.000671819
ENSG00000131042	LILRB2	1.458348537	1.08064E−05
ENSG00000182472	CAPN12	1.45730071	0.0001162
ENSG00000106123	EPHB6	1.456289268	0.00039008
ENSG00000169862	CTNND2	1.455089876	0.001836041
ENSG00000196092	PAX5	1.454324621	0.049558989
ENSG00000119535	CSF3R	1.453178275	2.59486E−06
ENSG00000172889	EGFL7	1.451660278	6.27202E−09
ENSG00000100628	ASB2	1.447979187	0.000189938
ENSG00000047617	ANO2	1.447971918	0.000188114
ENSG00000188290	HES4	1.44527957	7.46094E−06
ENSG00000108798	ABI3	1.445012041	5.35764E−08
ENSG00000167701	GPT	1.444221162	1.88403E−05
ENSG00000158571	PFKFB1	1.443803865	0.001480445
ENSG00000188820	FAM26F	1.443616952	0.000454748
ENSG00000136546	SCN7A	1.441838627	0.013750712
ENSG00000182511	FES	1.441405484	4.76048E−07
ENSG00000135744	AGT	1.440999485	0.010848761
ENSG00000157551	KCNJ15	1.439531321	0.001364319
ENSG00000204682	CASC10	1.439011293	0.000253335
ENSG00000005844	ITGAL	1.438845566	4.87749E−06
ENSG00000087258	GNAO1	1.438412397	6.97306E−05
ENSG00000043039	BARX2	1.43741433	0.005788686
ENSG00000182162	P2RY8	1.437004206	2.87771E−06
ENSG00000029534	ANK1	1.436837917	1.12422E−05
ENSG00000144891	AGTR1	1.436715397	0.020393409
ENSG00000101605	MYOM1	1.435106967	0.000223748
ENSG00000189350	FAM179A	1.434943722	2.53473E−06
ENSG00000100385	IL2RB	1.434556638	4.96027E−06
ENSG00000166816	LDHD	1.433738263	0.000243597
ENSG00000142156	COL6A1	1.433101784	4.66917E−07
ENSG00000010327	STAB1	1.431917332	2.04579E−07

TABLE 3B-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000036473	OTC	1.430512453	0.045203191
ENSG00000154451	GBPS	1.430340878	0.000634328
ENSG00000132938	MTUS2	1.425975562	0.011604099
ENSG00000007933	FMO3	1.423946685	0.001203078
ENSG00000149131	SERPING1	1.422621932	0.000396357
ENSG00000172828	CES3	1.419384028	0.000655981
ENSG00000171608	PIK3CD	1.41905466	3.53588E−07
ENSG00000064300	NGFR	1.417992298	0.000350911
ENSG00000118514	ALDH8A1	1.417317924	0.006378936
ENSG00000167286	CD3D	1.416497792	0.001019335
ENSG00000135519	KCNH3	1.415735452	0.00145232
ENSG00000169856	ONECUT1	1.412136864	0.010666397
ENSG00000160870	CYP3A7	1.408712629	0.024446748
ENSG00000050730	TNIP3	1.406955332	0.000669154
ENSG00000140538	NTRK3	1.40651603	0.000794662
ENSG00000171759	PAH	1.404407736	0.025034659
ENSG00000130303	BST2	1.403284722	3.13548E−05
ENSG00000124253	PCK1	1.402736368	0.028467751
ENSG00000135439	AGAP2	1.399151069	6.57005E−06
ENSG00000137265	IRF4	1.398129085	0.000204594
ENSG00000139144	PIK3C2G	1.395418582	0.039355522
ENSG00000106333	PCOLCE	1.395255366	2.75062E−08
ENSG00000163239	TDRD10	1.395113098	8.1805E−05
ENSG00000140853	NLRC5	1.394013874	1.3912E−05
ENSG00000159753	RLTPR	1.392255618	0.001169798
ENSG00000175489	LRRC25	1.391156103	2.68833E−06
ENSG00000135114	OASL	1.390001261	0.00059017
ENSG00000185215	TNFAIP2	1.389383822	4.1407E−06
ENSG00000139344	AMDHD1	1.387981179	0.03684003
ENSG00000153093	ACOXL	1.387844601	0.005899064
ENSG00000198821	CD247	1.387820922	0.000154722
ENSG00000169085	C8orf46	1.387524713	0.006875701
ENSG00000100368	CSF2RB	1.384962825	7.8841E−07
ENSG00000167895	TMC8	1.384767221	3.27719E−05
ENSG00000155657	TTN	1.383979127	0.000246024
ENSG00000141622	RNF165	1.383144496	0.003791615
ENSG00000162552	WNT4	1.378701388	4.52634E−05
ENSG00000185905	C16orf54	1.37848352	2.21048E−05
ENSG00000176383	B3GNT4	1.378040428	0.000189887
ENSG00000110777	POU2AF1	1.376583458	0.001575907
ENSG00000169248	CXCL11	1.376451509	0.016253559
ENSG00000183615	FAM167B	1.374963365	6.58579E−06
ENSG00000123329	ARHGAP9	1.374840469	2.56953E−06
ENSG00000205436	EXOC3L4	1.374064892	2.26388E−08
ENSG00000143869	GDF7	1.373721574	0.001414276
ENSG00000042781	USH2A	1.373645934	0.007969349
ENSG00000166428	PLD4	1.373505959	3.55186E−05
ENSG00000020633	RUNX3	1.371645797	1.88926E−07
ENSG00000174175	SELP	1.370020088	0.000587098
ENSG00000148803	FUOM	1.367938366	2.11789E−06
ENSG00000126709	IFI6	1.366363786	0.000985708
ENSG00000177807	KCNJ10	1.366234564	0.006225239
ENSG00000269404	SPIB	1.364097082	0.00156549
ENSG00000160323	ADAMTS13	1.363633887	9.78244E−06
ENSG00000169710	FASN	1.361278264	4.1289E−08
ENSG00000125910	S1PR4	1.360852503	0.00025185
ENSG00000110719	TCIRG1	1.358038633	4.78837E−08
ENSG00000134539	KLRD1	1.355600234	0.000299136
ENSG00000127954	STEAP4	1.354701727	0.001339098
ENSG00000104903	LYL1	1.353724395	1.84304E−07
ENSG00000162894	FAIM3	1.352538626	0.000188982
ENSG00000169418	NPR1	1.352033962	0.00015855
ENSG00000158786	PLA2G2F	1.351553394	0.005457894
EN5G00000077984	CST7	1.350919972	0.003159923
ENSG00000137877	SPTBN5	1.350588945	0.00110595
EN5G00000159189	C1QC	1.3498868	1.58024E−05
ENSG00000127528	KLF2	1.349131569	1.46824E−06
EN5G00000015285	WAS	1.348736349	3.7502E−06
EN5G00000169750	RAC3	1.347394699	1.40004E−05
ENSG00000117643	MAN1C1	1.346757216	3.86305E−06
ENSG00000159403	C1R	1.346255133	0.000342542
ENSG00000160326	SLC2A6	1.344283779	2.73676E−06
ENSG00000123360	PDE1B	1.343772761	4.91224E−06
ENSG00000112936	C7	1.343573236	0.024446748
ENSG00000135063	FAM189A2	1.342142585	0.002592105

TABLE 3B-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000116176	TPSG1	1.340310765	0.005059233
ENSG00000189056	RELN	1.339749907	0.00342347
ENSG00000101445	PPP1R16B	1.338140508	1.243E−05
ENSG00000169903	TM4SF4	1.33728372	0.023002889
ENSG00000154133	ROBO4	1.335671373	4.17897E−07
ENSG00000130489	SCO2	1.331302036	1.01974E−07
ENSG00000171049	FPR2	1.3312927	0.003415446
ENSG00000198753	PLXNB3	1.330747625	0.012771388
EN5G00000204577	LILRB3	1.330242639	2.17679E−05
ENSG00000179044	EXOC3L1	1.329930893	1.02312E−06
ENSG00000105227	PRX	1.326965637	1.21468E−06
ENSG00000163395	IGFN1	1.326541078	0.010632208
ENSG00000186827	TNFRSF4	1.322769209	1.07579E−05
ENSG00000157734	SNX22	1.32193201	0.00142706
ENSG00000144648	ACKR2	1.321631463	9.88382E−05
EN5G00000089820	ARHGAP4	1.32092602	7.86819E−06
ENSG00000175262	C1orf127	1.320722032	0.001786508
ENSG00000152784	PRDM8	1.31985205	7.7156E−05
ENSG00000198598	MMP17	1.318597563	0.036850845
ENSG00000172673	THEMIS	1.318181784	0.000493136
ENSG00000013725	CD6	1.31619461	5.66554E−05
ENSG00000241635	UGT1A1	1.31614142	0.028644359
ENSG00000143028	SYPL2	1.315335386	0.000128952
ENSG00000122490	PQLC1	1.3140364	1.54159E−09
ENSG00000137825	ITPKA	1.313445676	0.000866035
ENSG00000167508	MVD	1.312584378	2.75893E−08
EN5G00000006638	TBXA2R	1.311844461	5.62888E−06
ENSG00000166897	ELFN2	1.31073156	0.031142854
ENSG00000132386	SERPINF1	1.310719711	0.000210727
ENSG00000186907	RTN4RL2	1.310690555	3.01527E−05
ENSG00000135929	CYP27A1	1.309960107	4.05725E−06
ENSG00000188157	AGRN	1.309823267	3.79E−08
ENSG00000198851	CD3E	1.309233136	0.000205617
ENSG00000204444	APOM	1.308606774	0.008652124
ENSG00000099958	DERL3	1.307484028	0.000674201
ENSG00000171130	ATP6V0E2	1.303641323	3.47728E−05
ENSG00000122122	SASH3	1.303562183	1.8073E−06
ENSG00000122971	ACADS	1.303201091	7.64985E−10
ENSG00000158717	RNF166	1.301732784	1.94568E−09
ENSG00000095321	CRAT	1.299698193	4.79614E−07
ENSG00000168995	SIGLEC7	1.299681	0.000168534
ENSG00000180447	GAS1	1.299034643	0.000512172
ENSG00000092929	UNC13D	1.298770733	0.000302272
ENSG00000169252	ADRB2	1.296270277	0.000337699
ENSG00000196218	RYR1	1.294363789	0.001141674
ENSG00000182871	COL18A1	1.294145625	5.30035E−06
ENSG00000081479	LRP2	1.292962974	0.014450832
ENSG00000141338	ABCA8	1.292590541	0.016007005
ENSG00000179403	VWA1	1.291929758	1.09581E−05
ENSG00000124334	IL9R	1.291031644	0.001017975
ENSG00000161405	IKZF3	1.290585177	0.000264059
ENSG00000126264	HCST	1.290384181	0.000289026
ENSG00000075399	VPS9D1	1.289396862	8.96158E−09
ENSG00000076662	ICAM3	1.289393988	1.75721E−08
ENSG00000170214	ADRA1B	1.288566885	0.004623661
ENSG00000173372	C1QA	1.288030022	0.000419427
ENSG00000185507	IRF7	1.287857093	8.25769E−07
ENSG00000197253	TPSB2	1.287847104	0.004754687
ENSG00000169220	RGS14	1.286980501	1.59818E−06
ENSG00000119714	GPR68	1.286839432	0.000234779
ENSG00000089558	KCNH4	1.286186482	0.003005539
ENSG00000105639	JAK3	1.28579567	3.54358E−06
ENSG00000148346	LCN2	1.285775626	0.022139553
ENSG00000070985	TRPM5	1.284113725	0.006536381
ENSG00000274286	ADRA2B	1.283875269	0.006677597
ENSG00000126882	FAM78A	1.283087195	1.02284E−06
ENSG00000185340	GAS2L1	1.282914186	5.31352E−09
ENSG00000205078	SYCE1L	1.28266468	0.000114747
ENSG00000125551	PLGLB2	1.282193221	0.017770393
ENSG00000021461	CYP3A43	1.282118341	0.024675843
ENSG00000122224	LY9	1.279929863	0.000453
ENSG00000159231	CBR3	1.278960636	0.000476315
ENSG00000196700	ZNF512B	1.278867404	4.6102E−06
ENSG00000135898	GPR55	1.27861113	0.029853596
ENSG00000138030	KHK	1.278576173	3.99403E−05

TABLE 3B-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000145649	GZMA	1.276984142	0.009737375
ENSG00000185386	MAPK11	1.276319561	5.04464E-07
ENSG00000169738	DCXR	1.2753609	1.5413E-06
ENSG00000142173	COL6A2	1.275131727	1.28826E-05
ENSG00000173581	CCDC106	1.272140387	5.49353E-06
ENSG00000185347	C14orf80	1.270216159	3.19395E-08
ENSG00000196169	KIF19	1.270058837	0.010790431
ENSG00000178685	PARP10	1.269021594	2.26146E-09
ENSG00000121807	CCR2	1.268453693	0.001794151
ENSG00000163492	CCDC141	1.268330074	0.002739587
ENSG00000100079	LGALS2	1.268198947	0.029705602
ENSG00000185924	RTN4RL1	1.267257666	0.04679419
ENSG00000116661	FBXO2	1.266954006	0.013783534
ENSG00000198959	TGM2	1.266576781	1.43366E-05
ENSG00000012124	CD22	1.266360544	8.00988E-05
ENSG00000141506	PIK3R5	1.266229852	8.88741E-06
ENSG00000105538	RASIP1	1.266170986	4.78102E-05
ENSG00000122025	FLT3	1.26489447	0.003175215
ENSG00000103254	FAM173A	1.264595232	5.26363E-09
ENSG00000156886	ITGAD	1.2610692	0.002119374
ENSG00000177706	FAM20C	1.260244979	1.25398E-06
ENSG00000188064	WNT7B	1.260152118	0.009699119
ENSG00000132622	HSPA12B	1.259050734	1.99475E-06
ENSG00000144331	ZNF385B	1.258917589	0.038403342
ENSG00000168140	VASN	1.256361222	1.40715E-06
ENSG00000173227	SYT12	1.255402275	0.000952545
ENSG00000128283	CDC42EP1	1.254646849	1.19128E-08
ENSG00000144649	FAM198A	1.253770609	0.005101862
ENSG00000108242	CYP2C18	1.252384579	0.049445495
ENSG00000243414	TICAM2	1.251576637	3.39174E-05
ENSG00000183186	C2CD4C	1.250886399	0.000615976
ENSG00000153563	CD8A	1.250678303	0.000488152
ENSG00000049089	COL9A2	1.250591387	0.001579205
ENSG00000157927	RADIL	1.248223524	0.000100417
ENSG00000133048	CHI3L1	1.245811801	0.021325178
ENSG00000161618	ALDH16A1	1.244370735	8.4127E-09
ENSG00000149781	FERMT3	1.243405838	1.43792E-07
ENSG00000123689	G0S2	1.242808848	0.00273989
ENSG00000250510	GPR162	1.240962742	8.85735E-05
ENSG00000087237	CETP	1.240660267	0.011419735
ENSG00000009950	MLXIPL	1.237482445	0.001141373
ENSG00000165886	UBTD1	1.236166956	3.20006E-07
ENSG00000214063	TSPAN4	1.235756555	4.7405E-06
ENSG00000143382	ADAMTSL4	1.235690029	1.66736E-05
ENSG00000196358	NTNG2	1.234298082	3.33722E-05
ENSG00000179761	PIPOX	1.232024601	0.007340453
ENSG00000184922	FMNL1	1.230287144	1.9695E-06
ENSG00000172602	RND1	1.228522457	0.001807763
ENSG00000115255	REEP6	1.228306019	0.000846713
ENSG00000213145	CRIP1	1.226925682	0.000207155
ENSG00000137078	SIT1	1.22673322	0.004366955
ENSG00000232810	TNF	1.226621359	0.001125236
ENSG00000108551	RASD1	1.225543767	0.011690412
ENSG00000244242	IFITM10	1.224034083	3.98716E-06
ENSG00000198691	ABCA4	1.223798301	0.009398914
ENSG00000163874	ZC3H12A	1.223246451	2.28949E-07
ENSG00000143878	RHOB	1.221639417	1.68701E-05
ENSG00000184113	CLDN5	1.218254387	0.000542657
ENSG00000104894	CD37	1.217712684	5.74712E-05
ENSG00000128016	ZFP36	1.216595371	5.72502E-06
ENSG00000197471	SPN	1.215716502	9.0198E-06
ENSG00000166289	PLEKHF1	1.213445619	9.3501E-05
ENSG00000111913	FAM65B	1.213112434	8.25317E-05
ENSG00000107736	CDH23	1.21124224	5.45205E-05
ENSG00000141497	ZMYND15	1.210263071	2.68191E-06
ENSG00000102032	RENBP	1.209315238	2.08456E-05
ENSG00000110448	CD5	1.208394398	0.001390494
ENSG00000235568	NFAM1	1.208350739	5.73402E-07
ENSG00000205795	CYS1	1.208277485	0.001457831
ENSG00000137857	DUOX1	1.208233759	0.007487157
ENSG00000132329	RAMP1	1.207596418	0.000151863
ENSG00000213203	GIMAP1	1.206650397	0.000188673
ENSG00000159335	PTMS	1.203464099	1.03003E-07
ENSG00000081052	COL4A4	1.202960631	0.000201211
ENSG00000168994	PXDC1	1.202678576	4.72077E-05

TABLE 3B-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000171777	RASGRP4	1.202265459	2.81665E-05
ENSG00000160654	CD3G	1.20196118	0.000365209
ENSG00000080573	COL5A3	1.200805737	6.07373E-06
ENSG00000091831	ESR1	1.200583376	0.000774744
ENSG00000171303	KCNK3	1.20014995	0.005928289
ENSG00000185274	WBSCR17	1.19994384	0.000845441
ENSG00000175287	PHYHD1	1.198776424	0.000837289
ENSG00000066336	SPI1	1.198381682	4.26718E-06
ENSG00000132837	DMGDH	1.19707948	0.041104751
ENSG00000163519	TRAT1	1.196156055	0.018935271
ENSG00000171700	RGS19	1.196010764	9.53999E-07
ENSG00000187583	PLEKHN1	1.195422572	1.02071E-05
ENSG00000179583	CIITA	1.195282259	0.000271761
ENSG00000197019	SERTAD1	1.193431276	1.29925E-07
ENSG00000144596	GRIP2	1.192904741	0.000998238
ENSG00000151651	ADAM8	1.191465884	0.000214876
ENSG00000167549	CORO6	1.191456288	0.001594523
ENSG00000139899	CBLN3	1.190828966	1.18604E-05
ENSG00000130052	STARD8	1.190480825	1.85432E-05
ENSG00000168993	CPLX1	1.190376407	0.002199554
ENSG00000125089	SH3TC1	1.189769624	1.16481E-06
ENSG00000181035	SLC25A42	1.189715251	2.93113E-07
ENSG00000095370	SH2D3C	1.189470049	6.05052E-07
ENSG00000165716	FAM69B	1.188838195	0.012226404
ENSG00000164344	KLKB1	1.188755753	0.029216703
ENSG00000140511	HAPLN3	1.188670216	3.4617E-05
ENSG00000204301	NOTCH4	1.186538696	2.33235E-08
ENSG00000126246	IGFLR1	1.186443876	0.001222
ENSG00000176533	GNG7	1.185998076	0.000123399
ENSG00000100342	APOL1	1.185024196	0.000193231
ENSG00000100918	REC8	1.184690164	3.76756E-08
ENSG00000127129	EDN2	1.184507462	0.014275303
ENSG00000235098	ANKRD65	1.184396682	0.003096456
ENSG00000114923	SLC4A3	1.183439405	0.000723447
ENSG00000091592	NLRP1	1.182959918	3.84042E-05
ENSG00000205560	CPT1B	1.182632796	1.32115E-05
ENSG00000146094	DOK3	1.181661839	3.28488E-07
ENSG00000114378	HYAL1	1.181384394	0.000113442
ENSG00000130201	EXOC3L2	1.181023012	8.10527E-06
ENSG00000066735	KIF26A	1.180397791	0.019796758
ENSG00000177294	FBXO39	1.179991347	0.000556418
ENSG00000172236	TPSAB1	1.178949031	0.00366878
ENSG00000184985	SORCS2	1.178037587	0.001641863
ENSG00000175920	DOK7	1.176041109	0.011281996
ENSG00000100299	ARSA	1.17508065	1.94568E-09
ENSG00000225614	ZNF469	1.175078359	1.37323E-05
ENSG00000173267	SNCG	1.174670869	0.003930678
ENSG00000170955	PRKCDBP	1.174293625	1.1794E-05
ENSG00000158050	DUSP2	1.173650189	0.002134271
ENSG00000102962	CCL22	1.173459271	0.015542899
ENSG00000205784	ARRDC5	1.172873645	0.001814455
ENSG00000134463	ECHDC3	1.172738848	0.03883662
ENSG00000138131	LOXL4	1.172728047	0.004815049
ENSG00000115590	IL1R2	1.172239851	0.000617956
ENSG00000173210	ABLIM3	1.172167801	0.003996414
ENSG00000099860	GADD45B	1.17198885	0.000336154
ENSG00000138623	SEMA7A	1.171977056	0.001270896
ENSG00000165644	COMTD1	1.17157671	3.14594E-06
ENSG00000138964	PARVG	1.170941194	2.2748E-05
ENSG00000261221	ZNF865	1.17089339	1.17477E-10
ENSG00000129450	SIGLEC9	1.17087874	1.09789E-05
ENSG00000173369	C1QB	1.170411294	0.001035201
ENSG00000269190	FBXO17	1.170232238	0.022139891
ENSG00000130307	USHBP1	1.170049949	0.000144128
ENSG00000205403	CFI	1.169992923	0.00248748
ENSG00000188897	CTD-3088G3.8	1.169677435	2.88291E-05
ENSG00000179862	CITED4	1.169301175	0.000543753
ENSG00000161243	FBXO27	1.168148306	0.024452406
ENSG00000186765	FSCN2	1.168084426	0.00024425
ENSG00000179388	EGR3	1.166963889	0.000671962
ENSG00000186265	BTLA	1.166027379	0.007645981
ENSG00000198844	ARHGEF15	1.166006227	1.4018E-05
ENSG00000181625	SLX1B	1.165410826	0.018464653
ENSG00000140859	KIFC3	1.165172611	1.50409E-05
ENSG00000099994	SUSD2	1.165085326	2.44696E-05

TABLE 3B-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000130758	MAP3K10	1.165018455	8.81112E−09
ENSG00000130775	THEMIS2	1.164140071	1.1141E−05
ENSG00000019169	MARCO	1.163899272	0.03788321
ENSG00000174562	KLK15	1.163514709	0.03074354
ENSG00000107562	CXCL12	1.163277714	0.003116543
ENSG00000276231	PIK3R6	1.16274259	2.5923E−06
ENSG00000100055	CYTH4	1.162660663	8.31237E−06
ENSG00000081041	CXCL2	1.162017607	0.001710475
ENSG00000188385	JAKMIP3	1.161023941	0.00025117
ENSG00000100726	TELO2	1.16019289	1.77681E−08
ENSG00000127084	FGD3	1.160181671	5.821E−06
ENSG00000170442	KRT86	1.160047609	0.010902873
ENSG00000146215	CRIP3	1.159728565	0.012036054
ENSG00000175040	CHST2	1.159387841	1.74927E−07
ENSG00000113263	ITK	1.157962814	0.002994329
ENSG00000066056	TIE1	1.157121327	2.57919E−06
ENSG00000064932	SBNO2	1.154842996	2.01349E−09
ENSG00000142303	ADAMTS10	1.154016736	3.50003E−06
ENSG00000121270	ABCC11	1.153425253	0.007349047
ENSG00000142347	MYO1F	1.153301943	2.80959E−06
ENSG00000211445	GPX3	1.152979864	0.002642485
ENSG00000139626	ITGB7	1.152816513	2.59729E−05
ENSG00000150051	MKX	1.152675665	0.003591418
ENSG00000106605	BLVRA	1.152291726	7.38312E−05
ENSG00000117984	CTSD	1.150406941	7.23012E−07
ENSG00000262814	MRPL12	1.14980132	1.01717E−06
ENSG00000037280	FLT4	1.149616206	1.91092E−05
ENSG00000049768	FOXP3	1.148572275	0.000210255
ENSG00000119673	ACOT2	1.148562993	1.96284E−05
ENSG00000244607	CCDC13	1.148402517	0.001083259
ENSG00000174004	NRROS	1.146957235	0.000398563
ENSG00000242114	MTFP1	1.146834792	0.000127226
ENSG00000234745	HLA-B	1.14449985	0.000192326
ENSG00000160712	IL6R	1.144394841	6.18274E−05
ENSG00000155666	KDM8	1.14393085	7.1391E−06
ENSG00000274897	PANO1	1.143671055	0.006883127
ENSG00000144712	CAND2	1.143301833	0.003189252
ENSG00000072163	LIMS2	1.14253052	5.08751E−06
ENSG00000180089	TMEM86B	1.142254851	3.58273E−05
ENSG00000136244	IL6	1.142155804	0.005306614
ENSG00000140564	FURIN	1.14099648	4.8433E−08
ENSG00000180448	HMHA1	1.140877238	3.16186E−07
ENSG00000041515	MYO16	1.137936033	0.014846776
ENSG00000108821	COL1A1	1.137906751	6.96901E−05
ENSG00000167617	CDC42EP5	1.137640568	2.06907E−05
ENSG00000110900	TSPAN11	1.137384026	0.01727461
ENSG00000153976	HS3ST3A1	1.136861692	0.00145564
ENSG00000159958	TNFRSF13C	1.135763754	0.000505142
ENSG00000136383	ALPK3	1.134521046	0.000911625
ENSG00000124507	PACSIN1	1.133485154	0.01802573
ENSG00000131355	EMR3	1.133123347	0.002138295
ENSG00000182866	LCK	1.132590929	0.001221493
ENSG00000137841	PLCB2	1.131199585	4.80977E−05
ENSG00000166741	NNMT	1.130139929	0.003612422
ENSG00000244617	ASPRV1	1.129943712	8.47997E−05
ENSG00000141753	IGFBP4	1.12987189	2.06992E−07
ENSG00000131584	ACAP3	1.128585412	5.13604E−08
ENSG00000186517	ARHGAP30	1.128385549	1.78438E−06
ENSG00000107281	NPDC1	1.128109941	0.000153557
ENSG00000224051	CPTP	1.127327512	7.12605E−08
ENSG00000137225	CAPN11	1.127116709	0.000800018
ENSG00000198355	PIM3	1.126715724	2.06238E−08
ENSG00000065054	SLC9A3R2	1.126549161	4.41674E−07
ENSG00000128815	WDFY4	1.126187069	3.84042E−05
ENSG00000160446	ZDHHC12	1.125407504	2.69962E−08
ENSG00000166250	CLMP	1.125265155	0.012732841
ENSG00000064687	ABCA7	1.124560595	2.12037E−06
ENSG00000177301	KCNA2	1.124375927	0.030590556
ENSG00000089847	ANKRD24	1.123147631	0.00010158
ENSG00000124780	KCNK17	1.123054975	0.039607548
ENSG00000183484	GPR132	1.122788398	0.000233572
ENSG00000177098	SCN4B	1.121852752	0.004936442
ENSG00000167646	DNAAF3	1.121818701	0.01541232
ENSG00000179344	HLA-DQB1	1.121194027	0.003860617
ENSG00000175756	AURKAIP1	1.120692217	5.56991E−08
ENSG00000128594	LRRC4	1.120596728	0.031922975
ENSG00000153902	LGI4	1.120555731	0.01945264
ENSG00000169026	MFSD7	1.120383414	4.02105E−05
ENSG00000196329	GIMAP5	1.119693858	0.004400199
ENSG00000147082	CCNB3	1.119606628	0.002188382
ENSG00000204936	CD177	1.119224649	0.008447061
ENSG00000164082	GRM2	1.118910518	0.000505892
ENSG00000174946	GPR171	1.118335829	0.04527799
ENSG00000100258	LMF2	1.116907105	1.61252E−09
ENSG00000138316	ADAMTS14	1.116832224	0.000353376
ENSG00000177103	DSCAML1	1.115647195	0.018105046
ENSG00000179094	PER1	1.115552017	1.65195E−05
ENSG00000171631	P2RY6	1.115532374	0.001882189
ENSG00000140678	ITGAX	1.115131768	0.000229531
ENSG00000108515	ENO3	1.114503016	1.00695E−05
ENSG00000186350	RXRA	1.114500407	3.56261E−09
ENSG00000172349	IL16	1.114433597	7.70443E−05
ENSG00000001630	CYP51A1	1.113923372	3.37844E−05
ENSG00000166819	PLIN1	1.11373741	0.000662335
ENSG00000213445	SIPA1	1.113237843	3.13066E−08
ENSG00000130592	LSP1	1.112880732	2.25894E−05
ENSG00000197483	ZNF628	1.112760768	6.95363E−09
ENSG00000232434	C9orf172	1.112181438	1.66071E−05
ENSG00000140691	ARMC5	1.111440744	6.03792E−08
ENSG00000184163	FAM132A	1.110471489	0.000926624
ENSG00000126603	GLIS2	1.110337998	5.2843E−05
ENSG00000115648	MLPH	1.108800611	0.006797003
ENSG00000100399	CHADL	1.10872322	0.000236686
ENSG00000143546	S100A8	1.108121715	0.018184067
ENSG00000132361	CLUH	1.107468616	1.70231E−07
ENSG00000167705	RILP	1.106984107	1.16038E−05
ENSG00000177943	MAMDC4	1.105766892	4.92773E−05
EN5G00000204389	HSPA1A	1.105573406	0.026955025
ENSG00000164406	LEAP2	1.105554855	0.00483751
EN5G00000090339	ICAM1	1.105299336	1.01699E−05
ENSG00000107738	C10orf54	1.104818641	4.21805E−07
EN5G00000075340	ADD2	1.104459077	0.019321465
EN5G00000205502	C2CD4B	1.103521648	0.006132399
ENSG00000142494	SLC47A1	1.10185006	0.003457899
ENSG00000167604	NFKBID	1.101651665	3.19923E−07
ENSG00000110876	SELPLG	1.101255733	3.92388E−05
ENSG00000138080	EMILIN1	1.100491411	7.37093E−05
EN5G00000239697	TNFSF12	1.100488267	1.02589E−06
EN5G00000099864	PALM	1.099080013	9.65948E−05
ENSG00000183287	CCBE1	1.098938707	0.003307171
ENSG00000117016	RIMS3	1.098925724	0.000159024
ENSG00000129911	KLF16	1.098914019	1.87301E−08
ENSG00000148832	PAOX	1.098751829	2.04579E−07
ENSG00000159069	FBXW5	1.098608594	1.24453E−08
ENSG00000115556	PLCD4	1.098338046	0.002321536
ENSG00000126461	SCAF1	1.097461767	7.64985E−10
ENSG00000108405	P2RX1	1.095392688	0.000560723
ENSG00000187796	CARD9	1.095357432	0.00020497
EN5G00000099365	STX1B	1.095014517	7.83139E−05
ENSG00000111863	ADTRP	1.094270076	0.002274409
ENSG00000080007	DDX43	1.094255237	0.033692994
ENSG00000168389	MFSD2A	1.093807606	0.000368653
ENSG00000188833	ENTPD8	1.092008372	0.004385372
ENSG00000105329	TGFB1	1.091719304	8.49811E−06
ENSG00000178175	ZNF366	1.090809513	0.000176135
ENSG00000173264	GPR137	1.090306677	1.61252E−09
ENSG00000164362	TERT	1.090135651	0.012315101
ENSG00000168394	TAP1	1.088779671	9.37046E−05
ENSG00000185522	LMNTD2	1.088505352	3.75729E−07
ENSG00000134326	CMPK2	1.088235158	0.000574024
ENSG00000171766	GATM	1.08705008	0.007418665
EN5G00000083454	P2RX5	1.08688171	0.005272454
ENSG00000125384	PTGER2	1.086778309	0.001099626
ENSG00000186810	CXCR3	1.086635323	2.41732E−05
ENSG00000166592	RRAD	1.086211138	0.005249801
EN5G00000087076	HSD17B14	1.086016867	0.0006444
ENSG00000170638	TRABD	1.085976717	1.1093E−08
ENSG00000172346	CSDC2	1.085401102	0.013051358
ENSG00000100365	NCF4	1.083411322	0.000882812
ENSG00000167261	DPEP2	1.082913732	8.40121E−05

TABLE 3B-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000132530	XAF1	1.082746903	0.001133135
ENSG00000244482	LILRA6	1.081344765	0.001907085
ENSG00000173208	ABCD2	1.080547139	0.016361716
ENSG00000127948	POR	1.080517393	1.98599E−06
ENSG00000168421	RHOH	1.080458885	0.000631768
ENSG00000205045	SLFN12L	1.079701747	0.000329739
ENSG00000185100	ADSSL1	1.079301793	7.89069E−05
ENSG00000184371	CSF1	1.078895296	1.15396E−05
ENSG00000079432	CIC	1.078272473	9.56751E−10
ENSG00000135636	DYSF	1.078190227	2.43404E−05
ENSG00000169129	AFAP1L2	1.077772049	0.000590772
ENSG00000149451	ADAM33	1.077718443	0.01593276
ENSG00000071655	MBD3	1.076724274	5.2406E−08
ENSG00000143851	PTPN7	1.076655864	0.00112032
ENSG00000160447	PKN3	1.076244771	0.000102006
ENSG00000100351	GRAP2	1.075498285	0.000247936
ENSG00000100060	MFNG	1.075446319	3.10163E−05
ENSG00000146112	PPP1R18	1.075439687	6.37535E−07
ENSG00000144857	BOC	1.075195822	0.000855281
ENSG00000164742	ADCY1	1.07511608	0.009076307
ENSG00000166405	RIC3	1.075107073	0.015776542
ENSG00000008517	IL32	1.075098165	2.3075E−06
ENSG00000069399	BCL3	1.07418887	1.97112E−07
ENSG00000007314	SCN4A	1.074153208	0.030157553
ENSG00000007264	MATK	1.073659668	0.003255642
ENSG00000177542	SLC25A22	1.073637351	1.28739E−07
ENSG00000114654	EFCC1	1.073143748	0.000577098
ENSG00000160471	COX6B2	1.072662335	0.002420663
ENSG00000132016	C19orf57	1.069884421	0.001051846
ENSG00000008513	ST3GAL1	1.069062286	6.28731E−05
ENSG00000258429	PDF	1.068805467	1.60914E−05
ENSG00000131196	NFATC1	1.068662284	0.000153644
ENSG00000168490	PHYHIP	1.067989173	0.000655414
ENSG00000132321	IQCA1	1.067262986	0.003653666
ENSG00000142694	EVA1B	1.066699002	3.79044E−05
ENSG00000179593	ALOX15B	1.066673812	0.017470576
ENSG00000069535	MAOB	1.066281127	0.01103073
ENSG00000021488	SLC7A9	1.065153217	0.040473085
ENSG00000104856	RELB	1.064842196	6.80014E−08
ENSG00000143502	SUSD4	1.064151902	0.020512908
ENSG00000197766	CFD	1.063499521	0.006661899
ENSG00000141873	SLC39A3	1.06286932	1.61252E−09
ENSG00000144655	CSRNP1	1.062852718	3.78207E−06
ENSG00000179431	FJX1	1.062736663	0.001746152
ENSG00000010295	IFFO1	1.06198314	3.08202E−06
ENSG00000154146	NRGN	1.061895795	0.000514682
ENSG00000255587	RAB44	1.061875177	0.002263706
ENSG00000136689	1L1RN	1.061614732	0.004473602
ENSG00000212123	PRR22	1.060148319	0.000329992
ENSG00000184986	TMEM121	1.060127995	0.004337306
ENSG00000156218	ADAMTSL3	1.059442455	0.009010825
ENSG00000104518	GSDMD	1.058899122	1.68397E−08
ENSG00000127586	CHTF18	1.05847033	1.92166E−06
ENSG00000169885	CALML6	1.058443891	0.006025347
ENSG00000185432	METTL7A	1.058210929	0.000931459
ENSG00000197859	ADAMTSL2	1.058191896	0.000680205
ENSG00000173535	TNFRSF10C	1.057654248	0.001415259
ENSG00000205744	DENND1C	1.057627265	2.07749E−05
ENSG00000178226	PRSS36	1.057624918	0.00016216
ENSG00000104951	IL4I1	1.057323492	0.005793889
ENSG00000160255	ITGB2	1.056839191	0.000161016
ENSG00000198719	DLL1	1.05599471	0.001184828
ENSG00000133800	LYVE1	1.055850159	0.043808287
ENSG00000100292	HMOX1	1.05514357	0.000370937
ENSG00000228300	C19orf24	1.054694366	3.91459E−08
ENSG00000250506	CDK3	1.054690478	8.09788E−05
ENSG00000213638	ADAT3	1.054231629	1.26392E−05
ENSG00000143819	EPHX1	1.053600025	0.001432138
ENSG00000157873	TNFRSF14	1.053508443	2.32105E−07
ENSG00000075618	FSCN1	1.053500204	0.000139237
ENSG00000239389	PCDHA13	1.053422679	0.021095719
ENSG00000166831	RBPMS2	1.053327917	0.000473809
ENSG00000154102	C16orf74	1.052542155	0.021325178
ENSG00000183918	SH2D1A	1.050176267	0.022002936
ENSG00000204103	MAFB	1.050165961	2.79729E−05
ENSG00000142185	TRPM2	1.050001696	4.60613E−06
ENSG00000187513	GJA4	1.049591295	0.000260326
ENSG00000171223	JUNB	1.049275198	4.53987E−05
ENSG00000162881	OXER1	1.048671881	0.002008756
ENSG00000117318	ID3	1.048359003	0.000365298
ENSG00000167964	RAB26	1.048012744	0.008594494
ENSG00000090975	PITPNM2	1.04785399	1.25695E−08
ENSG00000088882	CPXM1	1.047614103	0.000275308
ENSG00000092295	TGM1	1.047489427	0.000318786
ENSG00000073169	SELO	1.047267301	1.04001E−08
ENSG00000198756	COLGALT2	1.046923157	0.017938451
ENSG00000196557	CACNA1H	1.046895388	0.000112454
ENSG00000204839	MROH6	1.046814689	0.00223642
ENSG00000142627	EPHA2	1.046491068	0.000121085
ENSG00000129968	ABHD17A	1.046154536	2.67234E−09
ENSG00000141968	VAV1	1.046065514	0.000227518
ENSG00000109956	B3GAT1	1.045800497	0.026258692
ENSG00000134824	FADS2	1.04551583	0.013619109
ENSG00000112195	TREML2	1.045199242	0.027528123
ENSG00000117090	SLAMF1	1.045027998	0.00104207
ENSG00000129467	ADCY4	1.044890545	1.88926E−07
ENSG00000110324	IL10RA	1.043561468	0.000159814
ENSG00000171703	TCEA2	1.042710176	7.3573E−05
ENSG00000257594	GALNT4	1.042103173	0.002255574
ENSG00000275074	NUDT18	1.041739758	1.09773E−07
ENSG00000132613	MTSS1L	1.041172779	2.38161E−05
ENSG00000177000	MTHFR	1.040644704	1.62671E−09
ENSG00000173918	C1QTNF1	1.040605797	2.45491E−06
ENSG00000059915	PSD	1.040036189	0.006261123
ENSG00000005381	MPO	1.039726111	0.018016543
ENSG00000188130	MAPK12	1.039036831	0.002218465
ENSG00000139865	TTC6	1.038538765	0.042982628
ENSG00000117594	HSD11B1	1.038346244	0.01897543
ENSG00000111186	WNT5B	1.038143085	0.045872871
ENSG00000140479	PCSK6	1.038010488	0.000125867
ENSG00000159674	SPON2	1.037337589	3.36554E−06
ENSG00000115607	IL18RAP	1.036524919	0.020819185
ENSG00000269313	MAGIX	1.035664732	0.000237527
ENSG00000171115	GIMAP8	1.034684315	0.00043775
ENSG00000167083	GNGT2	1.03468063	0.001995109
ENSG00000040487	PQLC2	1.034389549	2.48735E−09
ENSG00000219200	RNASEK	1.033863267	1.99409E−06
ENSG00000007171	NOS2	1.033693076	0.029503201
ENSG00000143845	ETNK2	1.033666496	0.014297837
ENSG00000169169	CPT1C	1.033096164	0.000280624
ENSG00000100003	SEC14L2	1.032643853	8.05301E−06
ENSG00000133561	GIMAP6	1.032162261	0.000410499
ENSG00000130748	TMEM160	1.031899717	3.04521E−05
ENSG00000176428	VPS37D	1.031638204	0.006069576
ENSG00000067840	PDZD4	1.031635532	0.001182899
ENSG00000260729	RP11-106M3.2	1.031523699	0.004422184
ENSG00000138615	CILP	1.031441487	0.004050808
ENSG00000136286	MYO1G	1.031431358	1.32038E−05
ENSG00000101306	MYLK2	1.03111681	0.015931012
ENSG00000130813	C19orf66	1.03098173	2.3625E−07
ENSG00000157881	PANK4	1.030716284	1.55066E−09
ENSG00000197943	PLCG2	1.03053882	3.32973E−05
ENSG00000088881	EBF4	1.030300777	7.54433E−05
ENSG00000169403	PTAFR	1.029756668	7.56013E−05
ENSG00000173156	RHOD	1.029683172	0.00046796
ENSG00000168685	IL7R	1.0288166	0.021919768
ENSG00000164877	MICALL2	1.028563364	1.53624E−06
ENSG00000198400	NTRK1	1.028519589	0.017969678
ENSG00000278272	HIST1H3C	1.02809485	0.04527799
ENSG00000135426	TESPA1	1.027798615	0.006769597
ENSG00000185112	FAM43A	1.02773188	0.000706383
ENSG00000133069	TMCC2	1.027431033	0.000504625
ENSG00000152669	CCNO	1.02741933	0.003849632
ENSG00000150281	CTF1	1.024938478	0.005641207
ENSG00000180340	FZD2	1.024674756	0.000793735
ENSG00000181847	TIGIT	1.024205903	0.005273732
ENSG00000167543	TP53I13	1.023958089	1.27231E−08
ENSG00000171119	NRTN	1.023021234	0.02325124
ENSG00000100242	SUN2	1.022893722	2.01349E−09
ENSG00000147813	NAPRT	1.022430177	6.39556E−06

TABLE 3B-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000117407	ARTN	1.022353399	0.0008376
ENSG00000105426	PTPRS	1.021824017	0.000212169
ENSG00000114270	COL7A1	1.021598787	0.001215547
ENSG00000153822	KCNJ16	1.021459687	0.044482696
ENSG00000077150	NFKB2	1.021430482	4.49101E-07
ENSG00000107404	DVL1	1.021045107	1.01962E-07
ENSG00000205220	PSMB10	1.021040341	3.62571E-05
ENSG00000125657	TNFSF9	1.019603439	0.031914053
ENSG00000078808	SDF4	1.019227571	2.01349E-09
ENSG00000154277	UCHL1	1.018802658	0.003540154
ENSG00000162490	DRAXIN	1.018565781	0.005194579
ENSG00000157103	SLC6A1	1.017456846	0.006172039
ENSG00000167700	MFSD3	1.017275872	4.18874E-06
ENSG00000174307	PHLDA3	1.017000493	0.001408229
ENSG00000142733	MAP3K6	1.016883678	8.16815E-06
ENSG00000139737	SLAIN1	1.016814932	0.015892184
ENSG00000213398	LCAT	1.01669424	0.000482415
ENSG00000107872	FBXL15	1.016569441	1.29236E-06
EN5G00000154783	FGD5	1.016439449	0.000753317
ENSG00000130881	LRP3	1.016427576	0.000308748
ENSG00000183307	CECR6	1.016246615	0.004475632
ENSG00000188566	NDOR1	1.015176081	1.74927E-07
ENSG00000040608	RTN4R	1.013297884	0.005004347
ENSG00000278817	DGCR6	1.013286788	0.00290828
ENSG00000128918	ALDH1A2	1.013137666	0.005867698
ENSG00000164867	NOS3	1.013029428	1.6008E-06
ENSG00000172382	PRSS27	1.012692081	0.005160783
ENSG00000172771	EFCAB12	1.011647683	0.000719841
ENSG00000175592	FOSL1	1.011353509	0.001165444
ENSG00000250588	IQCJ-SCHIP1	1.010670959	0.002552664
ENSG00000158246	FAM46B	1.010098634	0.009784986
ENSG00000000938	FGR	1.009675657	0.000350001
ENSG00000111077	TNS2	1.009082599	1.60914E-05
ENSG00000091262	ABCC6	1.008007735	0.001454326
ENSG00000179921	GPBAR1	1.007582784	0.000895708
ENSG00000187556	NANOS3	1.007482149	0.005960624
ENSG00000163599	CTLA4	1.007446501	0.034491458
ENSG00000173269	MMRN2	1.007103915	7.63617E-06
ENSG00000099957	P2RX6	1.005774931	0.014788148
ENSG00000075702	WDR62	1.005394304	3.82812E-05
ENSG00000140254	DUOXA1	1.005197626	0.030157553
ENSG00000160408	ST6GALNAC6	1.004182254	6.00075E-07
ENSG00000162591	MEGF6	1.003455165	0.000102697
ENSG00000099998	GGT5	1.002930452	0.000349259
ENSG00000124126	PREX1	1.002854047	9.05886E-06
ENSG00000132879	FBXO44	1.00159982	4.6691E-05
ENSG00000179023	KLHDC7A	1.000944037	0.044341993
ENSG00000153233	PTPRR	-1.001554855	0.033837303
ENSG00000076053	RBM7	-1.001759951	6.95363E-09
ENSG00000272602	ZNF595	-1.002136961	0.000561463
ENSG00000120256	LRP11	-1.002266863	1.70427E-06
ENSG00000137831	UACA	-1.003056551	6.66332E-08
ENSG00000104412	EMC2	-1.003528223	2.00163E-07
ENSG00000085719	CPNE3	-1.004877956	1.29006E-06
ENSG00000168152	THAP9	-1.004879803	8.60975E-07
ENSG00000170759	KIF5B	-1.007465609	1.99409E-06
ENSG00000101928	MOSPD1	-1.008717348	5.821E-06
ENSG00000144895	EIF2A	-1.009295057	6.56118E-09
ENSG00000162980	ARL5A	-1.009810828	3.56622E-09
ENSG00000170647	TMEM133	-1.010755081	1.40464E-06
ENSG00000176731	C8orf59	-1.011266379	2.72451E-07
ENSG00000173467	AGR3	-1.012732957	0.038558978
ENSG00000113494	PRLR	-1.01466158	0.000333796
ENSG00000167232	ZNF91	-1.016817351	7.07164E-08
ENSG00000128609	NDUFA5	-1.019382369	1.27231E-08
ENSG00000158290	CUL4B	-1.019448197	2.48735E-09
ENSG00000031691	CENPQ	-1.019776978	0.000122089
ENSG00000169446	MMGT1	-1.020403146	6.37063E-09
ENSG00000121957	GPSM2	-1.020454851	0.000162521
ENSG00000127995	CASD1	-1.020493061	1.01688E-06
ENSG00000149050	ZNF214	-1.021570453	2.23608E-05
ENSG00000110723	EXPH5	-1.022006186	4.71212E-05
ENSG00000272398	CD24	-1.024145293	0.002898564
ENSG00000281593	GS1-114I9.3	-1.0242454	0.000750007
ENSG00000205133	TRIQK	-1.024705878	1.81165E-07

TABLE 3B-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000001561	ENPP4	-1.025669868	3.20006E-07
ENSG00000151846	PABPC3	-1.025857769	1.83273E-05
ENSG00000241186	TDGF1	-1.025932935	0.003572067
ENSG00000170231	FABP6	-1.028359134	0.027437455
ENSG00000172292	CERS6	-1.030789935	2.82194E-08
ENSG00000085365	SCAMP1	-1.033529302	1.94568E-09
ENSG00000135338	LCA5	-1.035563463	2.38152E-05
ENSG00000176563	CNTDI	-1.036449608	0.030900597
ENSG00000147654	EBAG9	-1.037428459	6.87837E-08
ENSG00000149212	SESN3	-1.037498892	0.000439262
ENSG00000114248	LRRC31	-1.038660117	0.002789137
ENSG00000164934	DCAF13	-1.039870112	1.5195E-07
ENSG00000175548	ALG10B	-1.043186279	0.000200663
ENSG00000142875	PRKACB	-1.043355361	0.00044685
ENSG00000183742	MACC1	-1.04566096	1.18699E-05
ENSG00000155850	SLC26A2	-1.047315134	0.034353852
ENSG00000165028	NIPSNAP3B	-1.049187677	0.00033694
ENSG00000156162	DPY19L4	-1.050491072	2.90403E-07
ENSG00000014123	UFL1	-1.052174033	2.79903E-10
ENSG00000112742	TTK	-1.052232254	6.83677E-05
ENSG00000137501	SYTL2	-1.055045818	2.08215E-05
ENSG00000163806	SPDYA	-1.055660565	5.33991E-07
ENSG00000162620	LRRIQ3	-1.058277612	0.004212656
ENSG00000151239	TWF1	-1.062799425	1.61252E-09
ENSG00000164414	SLC35A1	-1.063652786	3.77487E-07
ENSG00000009844	VTA1	-1.068127232	1.52318E-09
ENSG00000175445	LPL	-1.068881665	0.003051402
ENSG00000104413	ESRP1	-1.069139697	3.22421E-06
ENSG00000180938	ZNF572	-1.071548068	4.8019E-05
ENSG00000137942	FNBP1L	-1.073865136	6.31494E-09
ENSG00000154153	FAM134B	-1.079187306	0.000616268
ENSG00000164754	RAD21	-1.080437352	3.40709E-07
ENSG00000101166	SLMO2	-1.083564414	1.20742E-07
ENSG00000180354	MTURN	-1.083961787	4.25839E-07
ENSG00000187325	TAF9B	-1.084956129	1.20282E-05
ENSG00000166323	C11orf65	-1.090229659	0.000165651
ENSG00000101132	PFDN4	-1.09076519	3.62677E-08
ENSG00000198478	SH3BGRL2	-1.092538935	4.66585E-08
ENSG00000241127	YAE1D1	-1.092681775	2.60598E-07
ENSG00000144362	PHOSPHO2	-1.099868358	1.20111E-07
ENSG00000023287	RB1CC1	-1.101297092	1.34567E-08
ENSG00000106819	ASPN	-1.107141062	0.000229665
ENSG00000106460	TMEM106B	-1.109324776	9.87742E-08
ENSG00000164176	EDIL3	-1.110129582	0.000472742
ENSG00000204899	MZT1	-1.113296799	6.92512E-07
ENSG00000137251	TINAG	-1.114764129	0.014297837
ENSG00000281760	AL138751.1	-1.118352932	0.00123223
ENSG00000112796	ENPP5	-1.118903111	6.8546E-05
ENSG00000152558	TMEM123	-1.124055055	1.45358E-08
ENSG00000184305	CCSER1	-1.129691637	0.002193699
ENSG00000255552	LY6G6E	-1.133450266	0.017549745
ENSG00000078114	NEBL	-1.134644322	4.2107E-07
ENSG00000114120	SLC25A36	-1.151854169	1.56096E-09
ENSG00000150783	TEX12	-1.153278512	0.003400066
ENSG00000280433	CH507-9B2.9	-1.157622705	2.1793E-07
ENSG00000183889	AC138969.4	-1.159897393	0.006281546
ENSG00000087253	LPCAT2	-1.167126908	1.09414E-05
ENSG00000213096	ZNF254	-1.169045539	1.02593E-08
ENSG00000203943	SAMD13	-1.169118931	5.54874E-06
ENSG00000124613	ZNF391	-1.169851393	2.08133E-06
ENSG00000139292	LGR5	-1.17614207	0.005411767
ENSG00000152580	IGSF10	-1.190907242	0.017317289
ENSG00000143882	ATP6V1C2	-1.19445769	0.02964975
ENSG00000104408	EIF3E	-1.195527466	1.08404E-07
ENSG00000000003	TSPAN6	-1.204923145	4.77464E-07
ENSG00000173890	GPR160	-1.20590218	0.000168715
ENSG00000134215	VAV3	-1.207076873	0.000113993
ENSG00000124205	EDN3	-1.212678763	0.032419727
ENSG00000250641	XXbac-BPG32J3.19	-1.216169136	0.021509264
ENSG00000213160	KLHL23	-1.219625769	2.1531E-08
ENSG00000267508	ZNF285	-1.221435784	0.040665124
ENSG00000124882	EREG	-1.221469332	0.005457894
ENSG00000168300	PCMTD1	-1.221506242	3.29417E-07
ENSG00000113389	NPR3	-1.224080887	0.000211447
ENSG00000104427	ZC2HC1A	-1.230963234	1.43368E-06

TABLE 3B-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000165730	STOX1	-1.267526619	0.015565296
ENSG00000253506	NACA2	-1.273329502	8.79573E−09
ENSG00000168772	CXXC4	-1.275875518	0.002203819
ENSG00000154639	CXADR	-1.285684188	6.95363E−09
ENSG00000087495	PHACTR3	-1.289857846	0.005176516
ENSG00000124429	POF1B	-1.303781347	2.38912E−07
ENSG00000196172	ZNF681	-1.305686053	0.000412086
ENSG00000259823	LYPD8	-1.308508498	0.013208003
ENSG00000072133	RPS6KA6	-1.316470671	0.000276829
ENSG00000178662	CSRNP3	-1.33898624	0.006283148
ENSG00000180785	OR51E1	-1.349625675	0.013011723
ENSG00000184434	LRRC19	-1.367459821	0.000306926
ENSG00000279342	AP000866.1	-1.386529623	1.96401E−08
ENSG00000204361	NXPE2	-1.43610326	0.003272598
ENSG00000145569	FAM105A	-1.447185798	1.27231E−08
ENSG00000164398	ACSL6	-1.499101213	0.001665712
ENSG00000146250	PRSS35	-1.520224914	0.000313552
ENSG00000164946	FREM1	-1.564863684	0.013976956
ENSG00000137968	SLC44A5	-1.598358074	0.000528403
ENSG00000095110	NXPE1	-1.615714581	0.030390621
ENSG00000101958	GLRA2	-1.616805688	0.041539661
ENSG00000151838	CCDC175	-1.737974925	0.000126766
ENSG00000181690	PLAG1	-1.751394808	0.000131268
ENSG00000007306	CEACAM7	-2.114674283	0.001548556

TABLE 3C

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000123500	COL10A1	2.753077645	1.94504E−10
ENSG00000135914	HTR2B	2.299775445	2.03486E−08
ENSG00000105664	COMP	2.250725891	2.79135E−07
ENSG00000113389	NPR3	2.24650213	9.31564E−11
ENSG00000111341	MGP	2.141302084	1.52321E−08
ENSG00000198542	ITGBL1	2.019042034	3.41856E−09
ENSG00000139329	LUM	2.0150524	3.41856E−09
ENSG00000011465	DCN	1.933536371	1.46255E−08
ENSG00000106483	SFRP4	1.9282142	2.31144E−07
ENSG00000044524	EPHA3	1.926985658	3.41856E−09
ENSG00000104435	STMN2	1.923594455	2.66078E−05
ENSG00000163145	C1QTNF7	1.922263003	3.25587E−07
ENSG00000171476	HOPX	1.919610126	1.64571E−09
ENSG00000170373	CST1	1.916865824	0.01433618
ENSG00000206052	DOK6	1.871623631	4.35587E−08
ENSG00000169604	ANTXR1	1.848403126	6.74299E−08
ENSG00000198523	PLN	1.843972102	2.56068E−06
ENSG00000170962	PDGFD	1.828019725	3.4197E−06
ENSG00000102452	NALCN	1.810294149	2.9295E−08
ENSG00000166448	TMEM130	1.809017594	4.29921E−06
ENSG00000164176	EDIL3	1.798363909	1.08047E−08
ENSG00000164220	F2RL2	1.795758993	4.16792E−07
ENSG00000163629	PTPN13	1.782990663	1.87323E−07
ENSG00000123096	SSPN	1.780091089	1.0293E−11
ENSG00000132031	MATN3	1.723529561	7.0153E−05
ENSG00000140937	CDH11	1.716527677	9.72444E−09
ENSG00000178662	CSRNP3	1.712333533	5.91801E−05
ENSG00000179542	SLITRK4	1.706883782	5.3193E−06
ENSG00000141469	SLC14A1	1.701274635	0.002158153
ENSG00000166923	GREM1	1.697378284	6.07649E−05
ENSG00000109738	GLRB	1.688798567	1.28131E−05
ENSG00000122641	INHBA	1.681574152	1.34487E−07
ENSG00000144810	COL8A1	1.660577626	4.3985E−08
ENSG00000050165	DKK3	1.656991196	7.88927E−08
ENSG00000180785	OR51E1	1.656338792	0.000523247
ENSG00000078098	FAP	1.648343594	3.41856E−09
ENSG00000134853	PDGFRA	1.64591078	2.42506E−07
ENSG00000106819	ASPN	1.624699824	3.2959E−08
ENSG00000130224	LRCH2	1.621049308	7.70087E−06
ENSG00000060709	RIMBP2	1.610582302	0.00442324
ENSG00000168334	XIRP1	1.607165827	0.00010874
ENSG00000134193	REG4	1.60569186	0.003181932
ENSG00000259030	FPGT-TNNI3K	1.605104369	3.3962E−07
ENSG00000139220	PPFIA2	1.60435623	2.03684E−05
ENSG00000116132	PRRX1	1.598455218	5.05329E−06
ENSG00000105989	WNT2	1.589894336	1.5746E−07
ENSG00000188783	PRELP	1.579932373	1.3397E−06
ENSG00000189320	FAM180A	1.579704065	9.56288E−06
ENSG00000101230	ISM1	1.57969389	1.82586E−06
ENSG00000123094	RASSF8	1.568362816	1.05386E−07
ENSG00000101825	MXRA5	1.55718306	1.54809E−05
ENSG00000170369	CST2	1.556271823	1.34657E−06
ENSG00000171016	PYGO1	1.550732543	2.41385E−07
ENSG00000171246	NPTX1	1.54930529	2.16518E−06
ENSG00000164197	RNF180	1.548429976	1.01886E−08
ENSG00000038427	VCAN	1.547202163	8.35279E−08
ENSG00000152583	SPARCL1	1.545464546	2.05733E−06
ENSG00000055732	MCOLN3	1.544706438	0.002283337
ENSG00000165617	DACT1	1.540192459	1.3355E−08
ENSG00000141052	MYOCD	1.533839495	1.27097E−06
ENSG00000189184	PCDH18	1.524966521	7.52638E−08
ENSG00000079931	MOXD1	1.52206901	8.62559E−07
ENSG00000138696	BMPR1B	1.520562773	1.46147E−05
ENSG00000164932	CTHRC1	1.517331528	1.98345E−08
ENSG00000109339	MAPK10	1.514795308	1.3355E−08
ENSG00000111799	COL12A1	1.514488875	9.54671E−06
ENSG00000170624	SGCD	1.513532236	1.34398E−07
ENSG00000182168	UNC5C	1.512500422	5.05212E−09
ENSG00000203805	PPAPDC1A	1.50990084	5.05862E−05
ENSG00000120337	TNFSF18	1.505492041	7.53394E−06
ENSG00000145687	SSBP2	1.498267108	1.64571E−09
ENSG00000079102	RUNX1T1	1.498049751	3.31914E−08
ENSG00000157680	DGKI	1.492753415	6.09951E−07
ENSG00000071967	CYBRD1	1.49130056	6.66385E−07
ENSG00000086991	NOX4	1.487601307	2.38406E−08
ENSG00000182013	PNMAL1	1.4704151	3.47752E−05
ENSG00000166928	MS4A14	1.460689948	1.28986E−06
ENSG00000158270	COLEC12	1.456479264	0.000123409
ENSG00000113578	FGF1	1.455640093	1.08615E−06
ENSG00000147027	TMEM47	1.454243074	1.55362E−07
ENSG00000137573	SULF1	1.450407418	5.42184E−06
ENSG00000061455	PRDM6	1.449956993	2.72945E−08
ENSG00000138685	FGF2	1.449712268	1.90869E−05
ENSG00000219438	FAM19A5	1.447573037	6.97472E−08
ENSG00000113361	CDH6	1.447278152	9.72444E−09
ENSG00000206538	VGLL3	1.446662197	1.24067E−08
ENSG00000269948	RP11−248J23.6	1.443017485	9.79357E−08
ENSG00000184838	PRR16	1.439275355	8.78211E−08
ENSG00000175445	LPL	1.431925332	7.82242E−06
ENSG00000123095	BHLHE41	1.431917846	7.90581E−08
ENSG00000120594	PLXDC2	1.429475002	1.56156E−07
ENSG00000132465	IGJ	1.42583631	0.001616392
ENSG00000006468	ETV1	1.423844057	9.72444E−09
ENSG00000163751	CPA3	1.42075873	8.80096E−05
ENSG00000082175	PGR	1.420382884	6.15718E−08
ENSG00000153956	CACNA2D1	1.419787753	1.01886E−08
ENSG00000273173	SNURF	1.418489439	0.000689692
ENSG00000171951	SCG2	1.417775686	0.001557801
ENSG00000253250	C8orf88	1.417096006	2.90069E−05
ENSG00000138061	CYP1B1	1.408888534	3.92298E−06
ENSG00000186310	NAP1L3	1.406286559	6.70314E−06
ENSG00000144642	RBMS3	1.406201717	6.71096E−08
ENSG00000117020	AKT3	1.404517394	5.08642E−08
ENSG00000118523	CTGF	1.400129682	1.57263E−06
ENSG00000112936	C7	1.390854001	0.009810176
ENSG00000172061	LRRC15	1.389505599	0.000484441
ENSG00000128045	RASL11B	1.385779054	0.000177713
ENSG00000164949	GEM	1.385443872	7.49878E−07
ENSG00000162998	FRZB	1.384895497	1.93262E−05
ENSG00000186479	RGS7BP	1.380174985	0.000292203
ENSG00000120820	GLT8D2	1.378308382	3.58732E−07
ENSG00000144619	CNTN4	1.377872505	4.0634E−07
ENSG00000104368	PLAT	1.369843778	6.09508E−07
ENSG00000170153	RNF150	1.362822582	8.14213E−06
ENSG00000180730	SHISA2	1.362386308	0.000271359
ENSG00000184226	PCDH9	1.361369498	8.92336E−07
ENSG00000136155	SCEL	1.358497995	0.013519504
ENSG00000112837	TBX18	1.357167308	0.015764677

TABLE 3C-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000173705	SUSD5	1.352563993	0.000866381
ENSG00000145431	PDGFC	1.352483377	1.10659E−07
ENSG00000091986	CCDC80	1.352248452	1.08521E−05
ENSG00000125869	LAMP5	1.348587285	1.38474E−05
ENSG00000181104	F2R	1.34574369	1.14245E−07
ENSG00000171817	ZNF540	1.34309348	1.67177E−05
ENSG00000174099	MSRB3	1.340803477	3.69366E−08
ENSG00000244694	PTCHD4	1.339435089	0.003004708
ENSG00000182050	MGAT4C	1.338163591	0.004097168
ENSG00000145244	CORIN	1.336481727	1.98313E−06
ENSG00000162493	PDPN	1.334674174	0.000278822
ENSG00000172348	RCAN2	1.334220756	5.21317E−06
ENSG00000106809	OGN	1.334183583	0.027938697
ENSG00000126860	EVI2A	1.334181518	3.75687E−05
ENSG00000117069	ST6GALNAC5	1.333984274	0.000168565
ENSG00000122786	CALD1	1.329513327	7.07147E−08
ENSG00000140285	FGF7	1.327620123	0.005858699
ENSG00000186354	C9orf47	1.327193509	0.000363669
ENSG00000143248	RGS5	1.326377353	3.48966E−05
ENSG00000162733	DDR2	1.325854104	6.97472E−08
ENSG00000118473	SGIP1	1.32523897	1.53101E−07
ENSG00000123610	TNFAIP6	1.318294514	4.38333E−05
ENSG00000114948	ADAM23	1.31458896	0.00040247
ENSG00000118922	KLF12	1.313963927	2.93943E−05
ENSG00000152527	PLEKHH2	1.307669268	5.05054E−06
ENSG00000166292	TMEM100	1.307432826	0.000384496
ENSG00000142871	CYR61	1.305804906	0.000113848
ENSG00000115380	EFEMP1	1.305757305	4.8433E−06
ENSG00000172403	SYNPO2	1.302382009	6.44659E−07
ENSG00000183801	OLFML1	1.301498794	3.03294E−06
ENSG00000182667	NTM	1.299038157	1.37123E−07
ENSG00000092969	TGFB2	1.298440651	8.81306E−07
ENSG00000102383	ZDHHC15	1.296671398	0.001991458
ENSG00000164935	DCSTAMP	1.293345365	0.000673846
ENSG00000148516	ZEB1	1.290822813	3.49298E−08
ENSG00000172476	RAB40A	1.290170038	0.000141934
ENSG00000280188	AC005477.1	1.289835364	0.009237267
ENSG00000121898	CPXM2	1.28965125	0.000314622
ENSG00000168461	RAB31	1.289572671	6.8273E−07
ENSG00000111339	ART4	1.289492512	0.000176902
ENSG00000168329	CX3CR1	1.286832974	8.8475E−05
ENSG00000186340	THBS2	1.286597108	5.35484E−06
ENSG00000184564	SLITRK6	1.285783204	0.03427456
ENSG00000007306	CEACAM7	1.284722771	0.01660678
ENSG00000143341	HMCN1	1.282445088	6.52761E−07
ENSG00000109684	CLNK	1.281226278	0.000311256
ENSG00000149380	P4HA3	1.280152222	3.99847E−07
ENSG00000183160	TMEM119	1.27777833	0.000796722
ENSG00000173068	BNC2	1.275532583	2.65783E−06
ENSG00000091844	RGS17	1.271354855	0.000336905
ENSG00000094963	FMO2	1.270693765	6.25198E−05
ENSG00000071991	CDH19	1.270654613	0.001176266
ENSG00000171659	GPR34	1.269314632	7.95073E−05
ENSG00000243244	STON1	1.269130245	2.70879E−08
ENSG00000169851	PCDH7	1.268726148	8.34772E−05
ENSG00000019991	HGF	1.268406656	6.34326E−05
ENSG00000122691	TWIST1	1.268232991	0.001671374
ENSG00000144681	STAC	1.267386375	0.00128752
ENSG00000162614	NEXN	1.26725904	7.42402E−07
ENSG00000125355	TMEM255A	1.265417711	0.000590037
ENSG00000048052	HDAC9	1.264177895	2.52719E−06
ENSG00000148053	NTRK2	1.262128711	0.005455326
ENSG00000106034	CPED1	1.260821872	3.2394E−05
ENSG00000106823	ECM2	1.259370731	7.44669E−07
ENSG00000188738	FSIP2	1.257352706	0.010675808
ENSG00000113209	PCDHB5	1.256678528	0.000940712
ENSG00000137558	PI15	1.255925384	0.000297298
ENSG00000196628	TCF4	1.254329918	3.03846E−07
ENSG00000115252	PDE1A	1.250018514	2.64199E−07
ENSG00000072952	MRVI1	1.249016956	7.43903E−07
ENSG00000198829	SUCNR1	1.248474774	0.000457552
ENSG00000134184	GSTM1	1.246483399	0.049619541
ENSG00000133107	TRPC4	1.245140196	1.38743E−05
ENSG00000166482	MFAP4	1.244718947	0.001246995
ENSG00000154188	ANGPT1	1.240410099	0.001977131

TABLE 3C-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000133110	POSTN	1.240025355	0.00049143
ENSG00000196569	LAMA2	1.238282396	0.00013276
ENSG00000116106	EPHA4	1.235126812	0.002447196
ENSG00000154263	ABCA10	1.235000212	4.01602E−06
ENSG00000164294	GPX8	1.234317717	1.67227E−07
ENSG00000110848	CD69	1.233437962	0.005637431
ENSG00000138135	CH25H	1.233435129	0.023392804
ENSG00000173641	HSPB7	1.233063449	9.60877E−05
ENSG00000169946	ZFPM2	1.23183164	1.27435E−06
ENSG00000112852	PCDHB2	1.231248693	0.001578874
ENSG00000123570	RAB9B	1.22728599	4.39928E−07
ENSG00000128606	LRRC17	1.226245678	9.09664E−06
ENSG00000129116	PALLD	1.225342682	1.55949E−07
ENSG00000166450	PRTG	1.224488053	0.000598677
ENSG00000139971	C14orf37	1.224263327	6.65939E−06
ENSG00000204442	FAM155A	1.222993304	0.018983556
ENSG00000119865	CNRIP1	1.219685116	3.34733E−07
ENSG00000156103	MMP16	1.218771751	2.31144E−07
ENSG00000131080	EDA2R	1.217055712	0.000101826
ENSG00000122877	EGR2	1.216936582	6.88846E−06
ENSG00000163453	IGFBP7	1.216563719	2.72187E−06
ENSG00000166432	ZMAT1	1.216400013	4.23217E−06
ENSG00000166086	JAM3	1.21607949	3.00641E−07
ENSG00000182263	FIGN	1.216012357	0.000149172
ENSG00000107518	ATRNL1	1.215303423	0.000179975
ENSG00000078018	MAP2	1.212839612	1.84683E−06
ENSG00000184156	KCNQ3	1.211113152	0.000813382
ENSG00000196381	ZNF781	1.210427458	0.000240218
ENSG00000197776	KLHDC1	1.209432681	5.69234E−07
ENSG00000164161	HHIP	1.209376306	6.71049E−05
ENSG00000171812	COL8A2	1.209367078	1.0172E−05
ENSG00000178033	FAM26E	1.20847607	7.80945E−08
ENSG00000160181	TFF2	1.20693478	0.007531691
ENSG00000106571	GLI3	1.206013848	4.88081E−06
ENSG00000129009	ISLR	1.205882434	1.38743E−05
ENSG00000135272	MDFIC	1.205668504	7.01323E−07
ENSG00000164418	GRIK2	1.203042047	0.006037303
ENSG00000152580	IGSF10	1.202815648	0.00626239
ENSG00000152402	GUCY1A2	1.202681424	1.27435E−06
ENSG00000100625	SIX4	1.202376393	0.007794779
ENSG00000151617	EDNRA	1.198067738	7.19393E−06
ENSG00000087245	MMP2	1.197459695	9.80267E−05
ENSG00000172915	NBEA	1.197191441	7.90995E−05
ENSG00000188921	PTPLAD2	1.196049296	3.32858E−06
ENSG00000147650	LRP12	1.194550854	6.66468E−06
ENSG00000013297	CLDN11	1.193131487	1.30641E−05
ENSG00000176971	FIBIN	1.191387166	4.62169E−06
ENSG00000196188	CTSE	1.19036335	0.02867178
ENSG00000124813	RUNX2	1.187351485	2.0362E−06
ENSG00000172201	ID4	1.185672386	9.67639E−05
ENSG00000134874	DZIP1	1.184217346	3.31914E−08
ENSG00000143387	CTSK	1.183440751	2.76708E−07
ENSG00000139174	PRICKLE1	1.183240996	3.24469E−06
ENSG00000134533	RERG	1.181677477	0.006782333
ENSG00000060718	COL11A1	1.181154156	0.000502238
ENSG00000145147	SLIT2	1.180183549	2.18991E−06
ENSG00000153292	GPR110	1.179913651	0.016985086
ENSG00000131459	GFPT2	1.177343428	3.92505E−05
ENSG00000173391	OLR1	1.176668514	0.000157527
ENSG00000211448	DIO2	1.176566161	0.002794342
ENSG00000145908	ZNF300	1.173849773	0.005884854
ENSG00000078589	P2RY10	1.173467703	0.001941456
ENSG00000002746	HECW1	1.172942469	0.00042753
ENSG00000122707	RECK	1.170766842	6.92282E−07
ENSG00000011201	KAL1	1.169712647	3.73246E−06
ENSG00000162692	VCAM1	1.168255525	4.87131E−05
ENSG00000138311	ZNF365	1.164097151	0.000503182
ENSG00000104447	TRPS1	1.162299394	1.02767E−06
ENSG00000171451	DSEL	1.161696195	5.38477E−06
ENSG00000170017	ALCAM	1.160712896	5.43327E−07
ENSG00000139926	FRMD6	1.160391169	6.3079E−07
ENSG00000073910	FRY	1.160163469	1.43319E−07
ENSG00000137273	FOXF2	1.157583315	0.000505777
ENSG00000136541	ERMN	1.155176394	0.000102981
ENSG00000182771	GRID1	1.150150735	0.001014429

TABLE 3C-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000171502	COL24A1	1.149995428	0.000173828
ENSG00000077264	PAK3	1.146860321	0.00406611
ENSG00000240038	AMY2B	1.145605746	2.51038E−06
ENSG00000163430	FSTL1	1.144209777	9.66921E−07
ENSG00000058091	CDK14	1.143535823	1.01886E−08
ENSG00000164764	SBSPON	1.143172285	0.045433189
ENSG00000146197	SCUBE3	1.142794148	0.009794541
ENSG00000115602	IL1RL1	1.142365242	0.003792042
ENSG00000090104	RGS1	1.140354037	0.000269751
ENSG00000149256	TENM4	1.140085482	6.3029E−05
ENSG00000138185	ENTPD1	1.136272638	7.44236E−07
ENSG00000137968	SLC44A5	1.134600285	0.002631951
ENSG00000144369	FAM171B	1.133531118	0.000171487
ENSG00000111087	GLI1	1.132278497	5.13596E−06
ENSG00000124491	F13A1	1.131386557	0.001904786
ENSG00000269920	RP11-690P14.4	1.131325905	0.000122922
ENSG00000115468	EFHD1	1.131079049	1.06566E−05
ENSG00000139278	GLIPR1	1.130826292	3.20069E−06
ENSG00000178343	SHISA3	1.130796631	0.000140736
ENSG00000258227	CLEC5A	1.130639256	6.68719E−05
ENSG00000166927	MS4A7	1.129035171	0.000106242
ENSG00000149212	SESN3	1.127242924	3.33122E−05
ENSG00000133392	MYH11	1.122036671	0.000620067
ENSG00000127863	TNFRSF19	1.121417576	0.03330431
ENSG00000120693	SMAD9	1.120809741	0.01515157
ENSG00000154654	NCAM2	1.119563764	0.001355873
ENSG00000117586	TNFSF4	1.118211022	2.97567E−06
ENSG00000183889	AC138969.4	1.11819356	0.003137054
ENSG00000115461	IGFBP5	1.116692007	0.000368757
ENSG00000162946	DISC1	1.115736631	2.73984E−06
ENSG00000254535	PABPC4L	1.115653577	7.85258E−05
ENSG00000154262	ABCA6	1.115587536	0.000547756
ENSG00000154258	ABCA9	1.115423601	0.00044798
ENSG00000173088	C10orf131	1.113938456	0.000278822
ENSG00000107186	MPDZ	1.110675366	9.6024E−06
ENSG00000204381	LAYN	1.106894012	1.03747E−05
ENSG00000138735	PDE5A	1.106156211	1.3397E−06
ENSG00000133104	SPG20	1.104999415	8.38798E−07
ENSG00000140092	FBLN5	1.103920818	0.000591908
ENSG00000115295	CLIP4	1.103736605	1.49464E−05
ENSG00000147138	GPR174	1.103719128	0.004945204
ENSG00000174740	PABPC5	1.103343026	0.000227181
ENSG00000196159	FAT4	1.101801065	5.63573E−05
ENSG00000116194	ANGPTL1	1.101127894	0.006070983
ENSG00000127990	SGCE	1.100578254	0.000718744
ENSG00000122870	BICC1	1.100576063	2.81243E−06
ENSG00000185008	ROB02	1.099265746	0.019037708
ENSG00000213694	S1PR3	1.09874409	3.48793E−05
ENSG00000067798	NAV3	1.098411466	0.000208293
ENSG00000106624	AEBP1	1.097916846	0.00045447
ENSG00000185052	SLC24A3	1.09641977	9.88467E−06
ENSG00000155754	ALS2CR11	1.095856973	0.000336063
ENSG00000119681	LTBP2	1.094933995	7.4972E−05
ENSG00000101134	DOK5	1.093841101	4.8433E−06
ENSG00000136546	SCN7A	1.092355329	0.035256333
ENSG00000170801	HTRA3	1.092109737	0.000182185
ENSG00000257242	C12orf79	1.091539632	0.003039378
ENSG00000154175	ABI3BP	1.089786874	0.000182124
ENSG00000143195	ILDR2	1.089285377	1.62346E−05
ENSG00000198300	PEG3	1.087321859	9.22214E−05
ENSG00000152495	CAMK4	1.084809673	0.000153038
ENSG00000185070	FLRT2	1.081974628	1.77411E−05
ENSG00000164694	FNDC1	1.081486749	0.000200727
ENSG00000178776	C5orf46	1.081247748	0.000128588
ENSG00000180044	C3orf80	1.080834073	0.000500175
ENSG00000149534	M54A2	1.080611922	0.000757529
ENSG00000053328	METTL24	1.079449984	0.000272257
ENSG00000073712	FERMT2	1.078621925	7.74666E−06
ENSG00000176928	GCNT4	1.075942338	3.80515E−05
ENSG00000184408	KCND2	1.075921601	0.000302824
ENSG00000071205	ARHGAP10	1.074797855	1.17758E−05
ENSG00000154553	PDLIM3	1.073477109	6.43903E−05
ENSG00000171533	MAP6	1.07252774	4.76448E−06
ENSG00000079150	FKBP7	1.072477835	2.45449E−08
ENSG00000111860	CEP85L	1.071194982	2.54905E−05

TABLE 3C-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000213949	ITGA1	1.068171951	2.75625E−07
ENSG00000206432	TMEM200C	1.068045023	0.000141934
ENSG00000022267	FHL1	1.067042498	4.62835E−05
ENSG00000182732	RGS6	1.065466272	0.015282834
ENSG00000155886	SLC24A2	1.064729282	0.032903108
ENSG00000168772	CXXC4	1.064636093	0.002123427
ENSG00000105971	CAV2	1.064015979	3.55749E−06
ENSG00000198046	ZNF667	1.062667648	1.58089E−05
ENSG00000174946	GPR171	1.062334847	0.034964856
ENSG00000151067	CACNA1C	1.060045584	1.51394E−05
ENSG00000183722	LHFP	1.059077805	5.41821E−06
ENSG00000061918	GUCY1B3	1.058644005	2.03083E−06
ENSG00000183578	TNFAIP8L3	1.0568722	0.00806722
ENSG00000130176	CNN1	1.055943534	3.11441E−05
ENSG00000169508	GPR183	1.055470175	0.004408157
ENSG00000069667	RORA	1.054780767	0.000126
ENSG00000163431	LMOD1	1.054106458	1.47358E−05
ENSG00000187955	COL14A1	1.049628519	0.000253813
ENSG00000184349	EFNA5	1.049530306	0.000219329
ENSG00000135046	ANXA1	1.049165077	7.85401E−05
ENSG00000124212	PTGIS	1.047840989	0.000371338
ENSG00000120658	ENOX1	1.044269556	0.000381683
ENSG00000124205	EDN3	1.043678212	0.029743438
ENSG00000203778	FAM229B	1.043236628	0.000285701
ENSG00000079257	LXN	1.041719528	2.97567E−06
ENSG00000151388	ADAMTS12	1.041086206	8.34369E−06
ENSG00000188171	ZNF626	1.040237517	0.000316508
ENSG00000166147	FBN1	1.038279431	4.43826E−06
ENSG00000121297	TSHZ3	1.038122506	1.06429E−06
ENSG00000151320	AKAP6	1.036943473	7.53394E−06
ENSG00000149970	CNKSR2	1.036454196	0.002094779
ENSG00000140538	NTRK3	1.035310447	0.004965763
ENSG00000113657	DPYSL3	1.035103238	4.08187E−05
ENSG00000161281	COX7A1	1.03502624	0.001537258
ENSG00000198795	ZNF521	1.033008485	6.55014E−05
ENSG00000091879	ANGPT2	1.032906302	8.72461E−05
ENSG00000172817	CYP7B1	1.031096543	0.000247574
ENSG00000170681	MURC	1.031087133	4.44393E−05
ENSG00000141431	ASXL3	1.03100311	0.002626424
ENSG00000175857	GAPT	1.030449253	0.000189649
ENSG00000137831	UACA	1.02949176	9.33137E−09
ENSG00000019549	SNAI2	1.028571266	1.29449E−05
ENSG00000175395	ZNF25	1.028531193	3.31914E−08
ENSG00000184304	PRKD1	1.027828768	1.13227E−06
ENSG00000042980	ADAM28	1.027310134	2.37072E−05
ENSG00000104332	SFRP1	1.027009502	0.000811385
ENSG00000185862	EVI2B	1.025232063	0.000259929
ENSG00000179909	ZNF154	1.024936412	2.34785E−06
ENSG00000137941	TTLL7	1.024753669	0.00048813
ENSG00000158186	MRAS	1.023633593	4.30876E−06
ENSG00000164107	HAND2	1.023465446	0.000341507
ENSG00000150076	CCDC7	1.023359419	1.25833E−05
ENSG00000079215	SLC1A3	1.022467446	0.001579851
ENSG00000180828	BHLHE22	1.021515955	0.005523297
ENSG00000170786	SDR16C5	1.020395127	0.028803293
ENSG00000144935	TRPC1	1.019616324	8.26821E−06
ENSG00000164116	GUCY1A3	1.019118915	8.58316E−06
ENSG00000147488	ST18	1.01841513	0.000537016
ENSG00000198846	TOX	1.015764922	0.010839842
ENSG00000114251	WNT5A	1.01566104	0.000106591
ENSG00000077092	RARB	1.015126049	4.34993E−06
ENSG00000129675	ARHGEF6	1.015044573	9.42125E−06
ENSG00000181264	TMEM136	1.014645604	4.0308E−05
ENSG00000133063	CHIT1	1.014438106	0.034967068
ENSG00000181007	ZFP82	1.013638458	0.001050926
ENSG00000030419	IKZF2	1.013441523	4.73393E−06
ENSG00000165028	NIPSNAP3B	1.011960146	6.97902E−05
ENSG00000165633	VSTM4	1.011056541	3.27269E−06
ENSG00000113580	NR3C1	1.00921802	9.2765E−06
ENSG00000162620	LRRIQ3	1.007955325	0.001693044
ENSG00000167757	KLK11	1.007520278	0.03319787
ENSG00000279342	AP000866.1	1.007380732	6.58012E−07
ENSG00000165072	MAMDC2	1.0071817	0.026128001
ENSG00000128739	SNRPN	1.006895383	0.00152501
ENSG00000153253	SCN3A	1.006646736	0.02899193

TABLE 3C-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000118526	TCF21	1.003870849	0.000290825
ENSG00000163563	MNDA	1.003220314	8.98979E−05
ENSG00000196664	TLR7	1.003111776	0.000586797
ENSG00000050555	LAMC3	1.001461135	0.015109089
ENSG00000090376	IRAK3	1.001220316	1.89957E−05
ENSG00000185112	FAM43A	−1.001751529	0.000376952
ENSG00000174276	ZNHIT2	−1.00469317	9.76788E−07
ENSG00000173825	TIGD3	−1.00548575	0.000430346
ENSG00000188486	H2AFX	−1.006974588	7.75283E−07
ENSG00000161888	SPC24	−1.007462984	1.17683E−05
ENSG00000103253	HAGHL	−1.008338066	0.000354038
ENSG00000100197	CYP2D6	−1.009743478	0.010379291
ENSG00000015520	NPC1L1	−1.012482977	0.024809378
ENSG00000092621	PHGDH	−1.01807365	0.035234547
ENSG00000204632	HLA-G	−1.019711771	0.009831723
ENSG00000009950	MLXIPL	−1.022450426	0.002998485
ENSG00000147813	NAPRT	−1.022826621	1.2798E−06
ENSG00000197785	ATAD3A	−1.023578406	4.62542E−08
ENSG00000076826	CAMSAP3	−1.024286378	1.14245E−07
ENSG00000125872	LRRN4	−1.027034577	0.032550873
ENSG00000245848	CEBPA	−1.028184918	2.88143E−07
ENSG00000261236	BOP1	−1.031422954	7.42402E−07
ENSG00000170684	ZNF296	−1.03381677	7.16344E−06
ENSG00000080854	IGSF9B	−1.039776887	0.025947588
ENSG00000100726	TELO2	−1.045077366	3.69366E−08
ENSG00000066735	KIF26A	−1.053439198	0.026280282
ENSG00000149150	SLC43A1	−1.053473873	1.32362E−05
ENSG00000169174	PCSK9	−1.054887434	0.007819461
ENSG00000168993	CPLX1	−1.055120067	0.003115199
ENSG00000172828	CES3	−1.055338797	0.004948623
ENSG00000149599	DUSP15	−1.058032584	0.022689093
ENSG00000186193	SAPCD2	−1.05890805	0.00011606
ENSG00000174669	SLC29A2	−1.06077456	1.58682E−06
ENSG00000132744	ACY3	−1.066735599	0.000490538
ENSG00000176919	C8G	−1.068239685	0.027915602
ENSG00000169683	LRRC45	−1.069647186	3.52775E−08
ENSG00000181790	BAI1	−1.071046307	0.003470875
ENSG00000124249	KCNK15	−1.074427039	0.011369482
ENSG00000132361	CLUH	−1.076184095	5.99561E−08
ENSG00000118160	SLC8A2	−1.08059558	0.010839842
ENSG00000083807	SLC27A5	−1.080803954	0.004509569
ENSG00000101412	E2F1	−1.083432202	3.46171E−06
ENSG00000120885	CLU	−1.084858207	0.038559395
ENSG00000244731	C4A	−1.088076152	0.039172855
ENSG00000130881	LRP3	−1.089753794	4.0074E−05
ENSG00000075702	WDR62	−1.090124394	2.74828E−06
ENSG00000168061	SAC3D1	−1.090353943	5.12645E−06
ENSG00000177602	GSG2	−1.090655414	0.000953296
ENSG00000162062	C16orf59	−1.091490514	2.36561E−05
ENSG00000104140	RHOV	−1.091638933	0.001003411
ENSG00000007216	SLC13A2	−1.093057698	0.048337224
ENSG00000262814	MRPL12	−1.097740165	6.58012E−07
ENSG00000155093	PTPRN2	−1.098512936	0.02196475
ENSG00000166391	MOGAT2	−1.099004103	0.007180743
ENSG00000137474	MY07A	−1.100568191	0.000105143
ENSG00000276043	UHRF1	−1.104503535	8.29192E−06
ENSG00000176428	VPS37D	−1.105348126	0.001507569
ENSG00000159423	ALDH4A1	−1.10814098	0.001116356
ENSG00000172782	FADS6	−1.110321794	0.047627443
ENSG00000140534	TICRR	−1.111545752	2.97061E−05
ENSG00000160867	FGFR4	−1.111845165	1.31042E−06
ENSG00000115718	PROC	−1.112809745	0.043806321
ENSG00000099769	IGFALS	−1.113018281	0.038559395
ENSG00000131188	PRR7	−1.114347592	9.94915E−07
ENSG00000166840	GLYATL1	−1.121036655	0.028826854
ENSG00000167700	MFSD3	−1.123728167	1.58464E−07
ENSG00000164620	RELL2	−1.126376462	3.14734E−05
ENSG00000162897	FCAMR	−1.126687354	0.003931285
ENSG00000177380	PPFIA3	−1.12968427	4.42898E−07
ENSG00000125144	MT1G	−1.13147587	0.030981806
ENSG00000170482	SLC23A1	−1.132254448	0.005223893
ENSG00000127564	PKMYT1	−1.132438141	1.43537E−06
ENSG00000183971	NPW	−1.133018221	0.004280082
ENSG00000160949	TONSL	−1.134113855	2.81623E−07
ENSG00000135097	MSI1	−1.13420336	0.035623024
ENSG00000160932	LY6E	−1.135450546	5.82577E−05
ENSG00000258429	PDF	−1.136902431	1.3397E−06
ENSG00000187017	ESPN	−1.138239397	0.000101684
ENSG00000167701	GPT	−1.141315424	0.000173096
ENSG00000167771	RCOR2	−1.141957361	0.001805997
ENSG00000189410	SH2D5	−1.145190586	0.022606753
ENSG00000169962	TAS1R3	−1.145928107	0.00728111
ENSG00000277363	SRCIN1	−1.147730626	4.18251E−05
ENSG00000204128	C2orf72	−1.148085566	0.001778856
ENSG00000111249	CUX2	−1.148558393	0.032607905
ENSG00000274267	HIST1H3B	−1.155845751	6.14265E−05
ENSG00000234602	MCIDAS	−1.157274122	0.007699226
ENSG00000185101	ANO9	−1.166208972	1.38743E−05
ENSG00000178821	TMEM52	−1.166457683	0.001754164
ENSG00000165716	FAM69B	−1.168533327	0.007163727
ENSG00000167900	TK1	−1.17018382	8.53148E−06
ENSG00000099617	EFNA2	−1.170438905	0.00048183
ENSG00000146670	CDCA5	−1.173617071	5.69234E−07
ENSG00000136457	CHAD	−1.182023544	0.023720863
ENSG00000136883	KIF12	−1.186005175	5.18794E−05
ENSG00000169710	FASN	−1.190277713	1.25719E−07
ENSG00000138030	KHK	−1.191482192	3.86632E−05
ENSG00000182327	GLTPD2	−1.196092546	0.016960088
ENSG00000260220	MGC50722	−1.197201902	0.026962886
ENSG00000168539	CHRM1	−1.198602912	0.022798841
ENSG00000186185	KIF18B	−1.20081172	1.97821E−06
ENSG00000137825	ITPKA	−1.201066297	0.000913212
ENSG00000280789	PAGR1	−1.214839339	7.72049E−05
ENSG00000173621	LRFN4	−1.214944868	1.55949E−07
ENSG00000164061	BSN	−1.215223715	0.025903361
ENSG00000177238	TRIM72	−1.222382743	0.023849438
ENSG00000167711	SERPINF2	−1.223629729	0.028145001
ENSG00000141505	ASGR1	−1.225548184	0.045750614
ENSG00000165644	COMTD1	−1.227602584	3.99847E−07
ENSG00000173894	CBX2	−1.234452318	0.000678006
ENSG00000181625	SLX1B	−1.234995479	0.006225067
ENSG00000171236	LRG1	−1.260424178	0.006121707
ENSG00000214456	PLIN5	−1.264174479	0.013042149
ENSG00000115290	GRB14	−1.267659636	0.026580911
ENSG00000089820	ARHGAP4	−1.269593592	3.23199E−06
ENSG00000102109	PCSK1N	−1.270769881	0.029488509
ENSG00000142748	FCN3	−1.272330535	0.020660974
ENSG00000198732	SMOC1	−1.272802772	0.036222164
ENSG00000187045	TMPRSS6	−1.27327971	0.016419753
ENSG00000089558	KCNH4	−1.29307111	0.001229742
ENSG00000139438	FAM222A	−1.29359271	0.000272257
ENSG00000181418	DDN	−1.298959188	2.05807E−05
ENSG00000273604	C17orf96	−1.299769213	1.93426E−05
ENSG00000105409	ATP1A3	−1.301076665	0.017641118
ENSG00000167676	PLIN4	−1.303896568	0.025372704
ENSG00000160957	RECQL4	−1.304548948	8.38587E−07
ENSG00000159650	UROC1	−1.306216441	0.019745439
ENSG00000187486	KCNJ11	−1.309606656	2.88429E−05
ENSG00000109758	HGFAC	−1.313280001	0.045084644
ENSG00000167992	VWCE	−1.318194033	0.005077692
ENSG00000127586	CHTF18	−1.319980205	6.94018E−09
ENSG00000166823	MESP1	−1.323889019	0.001845967
ENSG00000053108	FSTL4	−1.34822064	0.035955607
ENSG00000123561	SERPINA7	−1.358842508	0.047539566
ENSG00000167513	CDT1	−1.369477799	2.41385E−07
ENSG00000160224	AIRE	−1.372022713	0.030742055
ENSG00000101057	MYBL2	−1.372454731	1.65526E−06
ENSG00000174990	CA5A	−1.38459883	0.009925098
ENSG00000166183	ASPG	−1.39727814	0.004509381
ENSG00000197165	SULT1A2	−1.404041006	0.00014855
ENSG00000173826	KCNH6	−1.418866587	0.024724912
ENSG00000160716	CHRNB2	−1.42788262	0.031135519
ENSG00000149927	DOC2A	−1.440224607	0.016348954
ENSG00000161944	ASGR2	−1.447757676	0.044823356
ENSG00000131910	NR0B2	−1.449023932	0.000708453
ENSG00000125462	C1orf61	−1.47103537	0.013708059
ENSG00000145850	TIMD4	−1.4882556	0.006886844
ENSG00000152669	CCNO	−1.495196794	1.20302E−05
ENSG00000008735	MAPK8IP2	−1.500321268	0.006921494
ENSG00000180767	CHST13	−1.509067755	0.005363605

TABLE 3C-continued

Ensembl ID	Gene Symbol	log2FC	adj P-Value
ENSG00000156222	SLC28A1	−1.509136305	0.018472246
ENSG00000162460	TMEM82	−1.530716421	0.003893738
ENSG00000103723	AP3B2	−1.531296828	0.022096857
ENSG00000188883	KLRG2	−1.53704878	0.018096135
ENSG00000198535	C2CD4A	−1.550299035	0.000264523
ENSG00000131187	F12	−1.550770758	0.000598677
ENSG00000167588	GPD1	−1.558848619	0.000851273
ENSG00000169750	RAC3	−1.576133554	2.74832E−07
ENSG00000259803	SLC22A31	−1.577099411	0.04584251
ENSG00000114113	RBP2	−1.577684832	0.008239525
ENSG00000277196	PRODH	−1.578341259	0.003279393
ENSG00000174672	BRSK2	−1.584357103	0.00110229
ENSG00000156564	LRFN2	−1.586216269	0.013302955
ENSG00000057593	F7	−1.588647623	0.019402994
ENSG00000197444	OGDHL	−1.591753059	0.007481313
ENSG00000060566	CREB3L3	−1.655731801	0.010903719
ENSG00000185686	PRAME	−1.668077149	0.029594841
ENSG00000112494	UNC93A	−1.670260488	0.009379115
ENSG00000141485	SLC13A5	−1.678473209	0.025092248
ENSG00000128564	VGF	−1.682031349	0.039393053
ENSG00000107147	KCNT1	−1.687512018	0.006545909
ENSG00000069482	GAL	−1.707460098	0.009620975
ENSG00000130054	FAM155B	−1.727654652	0.014942749
ENSG00000139269	INHBE	−1.741155005	0.009647956
ENSG00000172482	AGXT	−1.749329793	0.026798512
ENSG00000105707	HPN	−1.794590272	0.007953985
ENSG00000120054	CPN1	−1.812734659	0.015558969
ENSG00000138308	PLA2G12B	−1.832138485	0.001435233
ENSG00000101204	CHRNA4	−1.858084234	0.004352226
ENSG00000196604	POTEF	−1.867424293	0.000555537
ENSG00000143627	PKLR	−1.868735021	0.002057997
ENSG00000177984	LCN15	−1.96847946	0.043777543
ENSG00000164362	TERT	−2.116087505	1.40839E−06
ENSG00000188176	SMTNL2	−2.218288559	0.000338971
ENSG00000159217	IGF2BP1	−2.756799479	0.036354585

[0124] Tables 4A-C: Differentially expressed miRNAs across SNF clusters in 93 metastatic miRNA samples identified by the limma method. (A) Differentially expressed miRNAs (DEMs) between SNF1 versus SNF2 and 3. (B) DEMs between SNF2 versus SNF1 and 3. (C) DEMs between SNF3 versus SNF1 and 2. Log 2FC: estimate of the log 2 fold-change corresponding to the contrast. Adj.P.Val: Benjamini-Hochberg corrected P-value. Cutoff values for DEGs are log 2FC=±1 and adj.P.Val≤0.05.

TABLE 4A

Differentially expressed miRNAs between SNF1 vs. SNF2 and SNF3

Probe Set Name	Transcript ID	log2FC	adj P-Val
MIMAT0000461_st	hsa-miR-195-5p	−1.016509129	5.74058E−06
MIMAT0000423_st	hsa-miR-125b-5p	−1.101525081	0.000255317
MIMAT0000451_st	hsa-miR-150-5p	−1.111931191	0.002189755
MIMAT0000098_st	hsa-miR-100-5p	−1.15185586	5.93555E−05
MIMAT0000097_st	hsa-miR-99a-5p	−1.37583683	0.000145126

TABLE 4B

Differentially expressed miRNAs between SNF2 vs. SNF1 and SNF3

Probe Set Name	Transcript ID	log2FC	adj P-Val
MIMAT0000421_st	hsa-miR-122-5p	2.240488686	0.003540262
MIMAT0019041_st	hsa-miR-4505	1.298904707	2.5899E−08
MIMAT0017990_st	hsa-miR-3613-5p	1.18902498	2.63247E−06
MIMAT0022967_st	hsa-miR-3620-5p	1.115649419	3.92575E−07
MIMAT0031002_st	hsa-miR-8075	1.080687514	8.01934E−07
MIMAT0019044_st	hsa-miR-4507	1.075979828	2.73172E−06
MIMAT0019069_st	hsa-miR-4530	1.051551622	3.22856E−07
MIMAT0010313_st	hsa-miR-762	1.019279452	2.73172E−06
MIMAT0022938_st	hsa-miR-937-5p	1.011491477	5.9441E−06
MIMAT0024616_st	hsa-miR-6132	1.002733507	1.39191E−07
MIMAT0000075_st	hsa-miR-20a-5p	−1.028612526	8.36836E−06
MIMAT0000078_st	hsa-miR-23a-3p	−1.112055891	1.11136E−08

TABLE 4C

Differentially expressed miRNAs between SNF3 vs. SNF1 and SNF2

Probe Set Name	Transcript ID	log2FC	adj P-Val
MIMAT0000232_st	hsa-miR-199a-3p	1.634106484	7.30981E−12
MIMAT0004563_st	hsa-miR-199b-3p	1.634106484	7.30981E−12
MIMAT0000461_st	hsa-miR-195-5p	1.42367983	6.10227E−12
MIMAT0000231_st	hsa-miR-199a-5p	1.37234542	8.05432E−10
MIMAT0000417_st	hsa-miR-15b-5p	1.207406832	3.95917E−09
MIMAT0000418_st	hsa-miR-23b-3p	1.158743828	8.45554E−10
MIMAT0000078_st	hsa-miR-23a-3p	1.104474733	5.56265E−10
MIMAT0000098_st	hsa-miR-100-5p	1.091350504	2.33107E−06
MIMAT0000082_st	hsa-miR-26a-5p	1.064950068	1.97806E−10
MIMAT0027430_st	hsa-miR-6765-5p	−1.00825087	5.76113E−09
MIMAT0019071_st	hsa-miR-4532	−1.013090134	1.59281E−05
MIMAT0016907_st	hsa-miR-4281	−1.013807197	7.45102E−08
MIMAT0028113_st	hsa-miR-7108-5p	−1.016242495	5.55427E−08
MIMAT0015082_st	hsa-miR-3197	−1.017126606	1.95996E−08
MIMAT0027600_st	hsa-miR-6850-5p	−1.020909622	1.21182E−08
MIMAT0027506_st	hsa-miR-6803-5p	−1.02336335	2.09619E−06
MIMAT0027616_st	hsa-miR-6858-5p	−1.023785192	2.81438E−08
MIMAT0018961_st	hsa-miR-4443	−1.039247982	5.53513E−09
MIMAT0019868_st	hsa-miR-4739	−1.039721011	1.11781E−09
MIMAT0015055_st	hsa-miR-3178	−1.050761351	1.01112E−08
MIMAT0023252_st	hsa-miR-5787	−1.055718868	3.79141E−07
MIMAT0019229_st	hsa-miR-3940-5p	−1.058608437	2.09139E−08
MIMAT0005922_st	hsa-miR-1268a	−1.062230989	1.97806E−10
MIMAT0022946_st	hsa-miR-1237-5p	−1.063146983	2.62774E−08
MIMAT0003326_st	hsa-miR-663a	−1.065257671	5.68431E−09
MIMAT0007347_st	hsa-miR-1469	−1.068502669	4.80996E−09
MIMAT0027510_st	hsa-miR-6805-5p	−1.071861119	1.66313E−08
MIMAT0027472_st	hsa-miR-6786-5p	−1.073166356	2.3974E−08
MIMAT0026486_st	hsa-miR-328-5p	−1.077373947	1.71028E−09
MIMAT0027526_st	hsa-miR-6813-5p	−1.078466785	8.45554E−10
MIMAT0004609_st	hsa-miR-149-3p	−1.081848255	2.21105E−09
MIMAT0019756_st	hsa-miR-4674	−1.090871453	5.538E−10
MIMAT0019913_st	hsa-miR-4763-3p	−1.093332207	1.94757E−08
MIMAT0005582_st	hsa-miR-1228-5p	−1.111569746	3.72512E−09
MIMAT0019027_st	hsa-miR-4492	−1.111808824	1.73716E−07
MIMAT0027482_st	hsa-miR-6791-5p	−1.114303081	6.60831E−08
MIMAT0019018_st	hsa-miR-4484	−1.124098667	3.55167E−09
MIMAT0024616_st	hsa-miR-6132	−1.125184942	5.56265E−10
MIMAT0019715_st	hsa-miR-4651	−1.125360214	6.43746E−09
MIMAT0023710_st	hsa-miR-6085	−1.126514316	1.11781E−09
MIMAT0024599_st	hsa-miR-6126	−1.128707561	3.45588E−06
MIMAT0027412_st	hsa-miR-6756-5p	−1.150459507	3.95917E−09
MIMAT0027532_st	hsa-miR-6816-5p	−1.162047562	5.56265E−10
MIMAT0010313_st	hsa-miR-762	−1.162936804	1.05505E−08
MIMAT0027458_st	hsa-miR-6779-5p	−1.190669994	1.85776E−09
MIMAT0019044_st	hsa-miR-4507	−1.193928349	2.3974E−08
MIMAT0022967_st	hsa-miR-3620-5p	−1.200066769	5.70033E−09
MIMAT0019077_st	hsa-miR-1587	−1.20141414	5.538E−10
MIMAT0019859_st	hsa-miR-4734	−1.202687453	1.53243E−09
MIMAT0022938_st	hsa-miR-937-5p	−1.214187024	1.05505E−08
MIMAT0019041_st	hsa-miR-4505	−1.30510348	1.03447E−09
MIMAT0018929_st	hsa-miR-4417	−1.346495056	3.31374E−07

[0125] Tables 5A-C: Ensemble of gene set enrichment analyses for hallmark mSigDB pathway signatures. Pathway enrichment or depletion (i.e., direction) was determined for each SNF cluster against the others (e.g., (SNF1−(SNF2+SNF3)/2)). The Hallmark Signature gene list was retrieved from Broad Institute's mSigDB. Twelve gene set enrichment algorithms (including GSVA, GAGE, PADOG, etc.) were used for analyses, and run independently for each set of gene lists. Results for SNF1 are set forth in Table 5A; results for SNF2 are test forth in Table 5B; and results for SNF3 are set forth in Table 5C. Raw P-values for a given pathway were combined across algorithms using Fisher's method and adjusted for multiple testing corrections by Bonferroni's method. Log 2 transformed fold-change (Log 2FC) was averaged in a similar fashion. A collective significance score proportional to combined P-values and average Log 2FC was generated and scaled from 0-100 to assess the degree of pathway enrichment or depletion relative to the inclusive set.

TABLE 5A

Ensemble of gene set enrichment for SNF1

	SNF1			
Hallmark Signature	Adj. P-value	Avg. Log2FC	Direction	Significance
HALLMARK_ADIPOGENESIS	0.562602325	0.23191575	+	0.126012262
HALLMARK_ALLOGRAFT_REJECTION	6.75282E−63	0.553139857	−	82.1598301
HALLMARK_ANDROGEN_RESPONSE	0.953425282	0.250863329	−	0
HALLMARK_ANGIOGENESIS	9.00116E−24	0.436617029	−	24.03100939
HALLMARK_APICAL_JUNCTION	7.93541E−21	0.364378219	−	17.48860976
HALLMARK_APICAL_SURFACE	8.1046E−12	0.373536233	−	9.887230372
HALLMARK_APOPTOSIS	6.12844E−09	0.332983644	−	6.522077617
HALLMARK_BILE_ACID_METABOLISM	8.64164E−12	0.304744608	−	8.043789379
HALLMARK_CHOLESTEROL_HOMEOSTASIS	0.679276374	0.259427257	−	0.091697977
HALLMARK_COAGULATION	8.574E−79	0.484603535	−	90.38557752
HALLMARK_COMPLEMENT	4.87698E−28	0.395441688	−	25.79468901
HALLMARK_DNA_REPAIR	6.06118E−18	0.237931563	+	9.776315817
HALLMARK_E2F_TARGETS	2.35724E−38	0.387862836	+	34.86066987
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION	1.18976E−77	0.54410568	−	100
HALLMARK_ESTROGEN_RESPONSE_EARLY	3.29177E−08	0.303711199	−	5.417803144
HALLMARK_ESTROGEN_RESPONSE_LATE	5.77006E−18	0.353150484	−	14.53457159
HALLMARK_FATTY_ACID_METABOLISM	0.505352718	0.239834804	+	0.157448737
HALLMARK_G2M_CHECKPOINT	1.14089E−30	0.37450212	+	26.78246369
HALLMARK_GLYCOLYSIS	0.028472201	0.262976639	+	0.958795842
HALLMARK_HEDGEHOG_SIGNALING	4.35218E−10	0.402046073	−	8.980849187
HALLMARK_HEME_METABOLISM	0.633625016	0.249634839	−	0.105790836
HALLMARK_HYPOXIA	0.000531718	0.294139451	−	2.28891919
HALLMARK_IL2_STAT5_SIGNALING	2.20482E−13	0.381886699	−	11.5369519
HALLMARK_IL6_JAK_STAT3_SIGNALING	4.37758E−25	0.496155656	−	28.86637252
HALLMARK_INFLAMMATORY_RESPONSE	1.72579E−64	0.53516896	−	81.52660353
HALLMARK_INTERFERON_ALPHA_RESPONSE	2.56172E−21	0.464322514	−	22.83372197
HALLMARK_INTERFERON_GAMMA_RESPONSE	5.73495E−41	0.508877735	−	48.9195911
HALLMARK_KRAS_SIGNALING_DN	1.19638E−56	0.416757758	−	55.67706303
HALLMARK_KRAS_SIGNALING_UP	1.77104E−57	0.472465669	−	64.05768668
HALLMARK_MITOTIC_SPINDLE	2.35806E−09	0.274931735	+	5.655361679
HALLMARK_MTORC1_SIGNALING	1.11639E−12	0.256734732	+	7.319839135
HALLMARK_MYC_TARGETS_V1	3.43273E−39	0.290461867	+	26.68402562
HALLMARK_MYC_TARGETS_V2	6.0312E−22	0.277009724	+	14.03310559
HALLMARK_MYOGENESIS	4.50624E−31	0.387783334	−	28.10652706
HALLMARK_NOTCH_SIGNALING	9.31025E−07	0.33759945	−	4.852771165
HALLMARK_OXIDATIVE_PHOSPHORYLATION	8.77461E−09	0.178039061	+	3.415120409
HALLMARK_P53_PATHWAY	1.08052E−05	0.286922361	−	3.392519492
HALLMARK_PANCREAS_BETA_CELLS	1.01417E−08	0.459352744	+	8.761839682
HALLMARK_PEROXISOME	0.431746974	0.242997597	+	0.199384512
HALLMARK_PI3K_AKT_MTOR_SIGNALING	0.233835825	0.252230734	+	0.367943227
HALLMARK_PROTEIN_SECRETION	0.431746974	0.169764376	+	0.135553192
HALLMARK_REACTIVE_OXIGEN_SPECIES_PATHWAY	0.496910388	0.242744195	+	0.163753185
HALLMARK_SPERMATOGENESIS	4.5866E−15	0.342373456	+	11.71790297
HALLMARK_TGF_BETA_SIGNALING	0.001440397	0.23403223	−	1.576612534
HALLMARK_TNFA_SIGNALING_VIA_NFKB	2.31011E−16	0.371786122	−	13.87862487
HALLMARK_UNFOLDED_PROTEIN_RESPONSE	4.75471E−17	0.231061775	+	8.999777787
HALLMARK_UV_RESPONSE_DN	2.36277E−07	0.334683613	−	5.287018314
HALLMARK_UV_RESPONSE_UP	0.073726326	0.314916265	−	0.839686559
HALLMARK_WNT_BETA_CATENIN_SIGNALING	0.00030316	0.296203452	−	2.477772217
HALLMARK_XENOBIOTIC_METABOLISM	8.85403E−21	0.302492803	−	14.48187852

TABLE 5B

Ensemble of gene set enrichment for SNF2

	SNF2			
Hallmark Signature	Adj. P-value	Avg. Log2FC	Direction	Significance
HALLMARK__ADIPOGENESIS	5.82382E−06	0.376237508	+	5.882317613
HALLMARK__ALLOGRAFT__REJECTION	1.45945E−40	0.543595115	+	72.99772011
HALLMARK__ANDROGEN__RESPONSE	2.99454E−12	0.370886686	−	13.73926065
HALLMARK__ANGIOGENESIS	0.00019338	0.411790376	−	4.381113101
HALLMARK__APICAL__JUNCTION	4.23961E−19	0.446257167	+	27.12128001
HALLMARK__APICAL__SURFACE	1.11488E−15	0.496384333	+	24.47343763
HALLMARK__APOPTOSIS	0.000198394	0.373000655	+	3.875844134
HALLMARK__BILE__ACID__METABOLISM	5.03525E−13	0.450256669	+	18.04634011
HALLMARK__CHOLESTEROL__HOMEOSTASIS	1.62885E−05	0.420630602	+	6.03405282
HALLMARK__COAGULATION	2.58606E−59	0.504790639	+	100
HALLMARK__COMPLEMENT	8.23511E−16	0.446198845	+	22.11507166
HALLMARK__DNA__REPAIR	3.14449E−07	0.368730815	−	7.342007266
HALLMARK__E2F__TARGETS	1.23697E−08	0.374919901	−	9.275439297
HALLMARK__EPITHELIAL__MESENCHYMAL__TRANSITION	1.9632E−21	0.407434289	+	27.93211451
HALLMARK__ESTROGEN__RESPONSE__EARLY	3.48034E−19	0.393898117	+	23.95655693
HALLMARK__ESTROGEN__RESPONSE__LATE	1.34211E−27	0.431906885	+	38.738538
HALLMARK__FATTY__ACID__METABOLISM	6.39585E−05	0.418958518	−	5.15824815
HALLMARK__G2M__CHECKPOINT	7.83336E−10	0.376504652	−	10.85654182
HALLMARK__GLYCOLYSIS	1.07007E−05	0.385285346	+	5.696741514
HALLMARK__HEDGEHOG__SIGNALING	0.063128326	0.342809773	−	0.569586763
HALLMARK__HEME__METABOLISM	1.91004E−08	0.416505838	−	10.12868816
HALLMARK__HYPOXIA	0.003124275	0.364832831	+	2.283534499
HALLMARK__IL2__STAT5__SIGNALING	2.10035E−05	0.406168105	+	5.645056887
HALLMARK__IL6__JAK__STAT3__SIGNALING	3.90097E−22	0.534823842	+	38.20549716
HALLMARK__INFLAMMATORY__RESPONSE	5.96656E−32	0.474979295	+	49.73266933
HALLMARK__INTERFERON__ALPHA__RESPONSE	2.06717E−21	0.544327528	+	37.55516943
HALLMARK__INTERFERON__GAMMA__RESPONSE	1.4102E−30	0.551942823	+	55.34125652
HALLMARK__KRAS__SIGNALING__DN	1.80809E−45	0.48049015	+	72.46554722
HALLMARK__KRAS__SIGNALING__UP	6.89314E−23	0.454194231	+	33.48581418
HALLMARK__MITOTIC__SPINDLE	4.86623E−17	0.40576277	−	21.73498143
HALLMARK__MTORC1__SIGNALING	2.36725E−09	0.359383083	−	9.736464696
HALLMARK__MYC__TARGETS__V1	2.47646E−17	0.336329169	−	18.20962527
HALLMARK__MYC__TARGETS__V2	0.071654539	0.34927155	+	0.530500529
HALLMARK__MYOGENESIS	5.11649E−22	0.466009232	+	32.99537081
HALLMARK__NOTCH__SIGNALING	0.127045562	0.27257069	−	0
HALLMARK__OXIDATIVE__PHOSPHORYLATION	4.53474E−05	0.312878012	−	3.800649111
HALLMARK__P53__PATHWAY	2.79313E−20	0.384211934	+	24.78207268
HALLMARK__PANCREAS__BETA__CELLS	1.32978E−08	0.514962394	−	12.99593374
HALLMARK__PEROXISOME	0.000540492	0.391346358	+	3.526670958
HALLMARK__PI3K__AKT__MTOR__SIGNALING	2.79466E−08	0.406359199	−	9.632656233
HALLMARK__PROTEIN__SECRETION	6.46486E−32	0.401763528	−	41.8905431
HALLMARK__REACTIVE__OXIGEN__SPECIES__PATHWAY	6.84591E−14	0.337891399	+	14.33325417
HALLMARK__SPERMATOGENESIS	8.98491E−25	0.399383156	−	31.91097763
HALLMARK__TGF__BETA__SIGNALING	3.39391E−07	0.358791161	−	7.081093476
HALLMARK__TNFA__SIGNALING__VIA__NFKB	5.51592E−08	0.401525725	+	9.103927568
HALLMARK__UNFOLDED__PROTEIN__RESPONSE	6.90293E−14	0.353336182	−	15.02213965
HALLMARK__UV__RESPONSE__DN	4.80807E−07	0.391600615	−	7.602798279
HALLMARK__UV__RESPONSE__UP	5.03525E−13	0.425384762	+	17.00347286
HALLMARK__WNT__BETA__CATENIN__SIGNALING	1.14962E−08	0.320004118	+	7.829567983
HALLMARK__XENOBIOTIC__METABOLISM	2.79972E−24	0.440206499	+	34.51707457

TABLE 5C

Ensemble of gene set enrichment for SNF3

	SNF3			
Hallmark Signature	Adj. P-value	Avg. Log2FC	Direction	Significance
HALLMARK__ADIPOGENESIS	1.55818E−08	0.347062376	+	5.830276063
HALLMARK__ALLOGRAFT__REJECTION	1.54771E−30	0.409633949	+	26.66786146
HALLMARK__ANDROGEN__RESPONSE	5.58612E−15	0.352177023	+	10.89597364
HALLMARK__ANGIOGENESIS	3.45876E−24	0.598625543	+	30.68790239
HALLMARK__APICAL__JUNCTION	0.014311071	0.392496006	+	1.475421281
HALLMARK__APICAL__SURFACE	0.008557246	0.355582565	−	1.500278679
HALLMARK__APOPTOSIS	0.24028799	0.3370387	+	0.345621249
HALLMARK__BILE__ACID__METABOLISM	6.40651E−17	0.452607089	−	15.96124558
HALLMARK__CHOLESTEROL__HOMEOSTASIS	1.50612E−08	0.414956169	−	7.00617984

TABLE 5C-continued

Ensemble of gene set enrichment for SNF3

	SNF3			
Hallmark Signature	Adj. P-value	Avg. Log2FC	Direction	Significance
HALLMARK_COAGULATION	7.28876E−78	0.591799104	+	100
HALLMARK_COMPLEMENT	3.31628E−14	0.383671799	+	11.22954857
HALLMARK_DNA_REPAIR	7.09556E−18	0.296873524	−	11.05288138
HALLMARK_E2F_TARGETS	4.01343E−05	0.317359552	−	2.947776837
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION	2.98646E−64	0.5504785	+	76.57662828
HALLMARK_ESTROGEN_RESPONSE_EARLY	1.95684E−11	0.335674703	−	7.770914865
HALLMARK_ESTROGEN_RESPONSE_LATE	1.26415E−28	0.3670826	−	22.34674831
HALLMARK_FATTY_ACID_METABOLISM	0.026445455	0.316655267	+	0.98347634
HALLMARK_G2M_CHECKPOINT	0.004086786	0.346547757	−	1.703232442
HALLMARK_GLYCOLYSIS	2.14691E−06	0.307696685	−	3.712745619
HALLMARK_HEDGEHOG_SIGNALING	2.66912E−06	0.472783662	+	5.666836546
HALLMARK_HEME_METABOLISM	1.62438E−10	0.308692274	+	6.515026382
HALLMARK_HYPOXIA	0.025953316	0.326899469	+	1.024768452
HALLMARK_IL2_STAT5_SIGNALING	0.035655456	0.360532179	+	1.032675815
HALLMARK_IL6_JAK_STAT3_SIGNALING	0.001256043	0.355292971	−	2.148273749
HALLMARK_INFLAMMATORY_RESPONSE	1.44422E−30	0.389268775	+	25.36214016
HALLMARK_INTERFERON_ALPHA_RESPONSE	0.664951063	0.288462241	−	0
HALLMARK_INTERFERON_GAMMA_RESPONSE	0.059074297	0.324142705	+	0.761258006
HALLMARK_KRAS_SIGNALING_DN	4.17203E−55	0.411178484	−	48.92382364
HALLMARK_KRAS_SIGNALING_UP	5.55843E−49	0.444215624	+	46.8972376
HALLMARK_MITOTIC_SPINDLE	2.77845E−06	0.332372127	−	3.937846618
HALLMARK_MTORC1_SIGNALING	3.81536E−05	0.315587428	−	2.945903414
HALLMARK_MYC_TARGETS_V1	0.03492292	0.23193917	−	0.628946187
HALLMARK_MYC_TARGETS_V2	2.22275E−30	0.368170912	−	23.83027384
HALLMARK_MYOGENESIS	5.219E−14	0.417339246	+	12.04454127
HALLMARK_NOTCH_SIGNALING	1.45209E−05	0.34372808	+	3.534839252
HALLMARK_OXIDATIVE_PHOSPHORYLATION	1.45209E−05	0.237455231	−	2.407287582
HALLMARK_P53_PATHWAY	3.00444E−06	0.294412433	−	3.453380966
HALLMARK_PANCREAS_BETA_CELLS	2.51102E−10	0.418358872	+	8.695839717
HALLMARK_PEROXISOME	0.002008089	0.279801031	−	1.542951276
HALLMARK_PI3K_AKT_MTOR_SIGNALING	2.46179E−05	0.346054892	+	3.385539093
HALLMARK_PROTEIN_SECRETION	5.94544E−28	0.330636676	+	19.62936657
HALLMARK_REACTIVE_OXIGEN_SPECIES_PATHWAY	1.6742E−11	0.229941171	−	5.322020787
HALLMARK_SPERMATOGENESIS	0.00097818	0.327090841	+	2.046742764
HALLMARK_TGF_BETA_SIGNALING	3.32207E−13	0.340143129	+	9.196290718
HALLMARK_TNFA_SIGNALING_VIA_NFKB	0.047592797	0.324563372	+	0.829197421
HALLMARK_UNFOLDED_PROTEIN_RESPONSE	3.21878E−06	0.29786512	+	3.475645011
HALLMARK_UV_RESPONSE_DN	4.6735E−31	0.418429487	+	27.7200871
HALLMARK_UV_RESPONSE_UP	1.06469E−15	0.347575215	−	11.30086584
HALLMARK_WNT_BETA_CATENIN_SIGNALING	0.044318157	0.276535424	−	0.708681745
HALLMARK_XENOBIOTIC_METABOLISM	3.63495E−34	0.433604847	−	31.68602021

Table 6: Ensemble of gene set enrichment analyses for custom colorectal cancer pathways. Pathway enrichment or depletion (i.e., direction) was determined for each SNF against the others (e.g., (SNF1−(SNF2+SNF3)/2)). A compilation of pathways associated immunology, metabolism, canonical pathways, cancer signatures, and stromal infiltration estimates were retrieved from[14]. Twelve gene set enrichment algorithms (including GSVA, GAGE, PADOG, etc.) were used for analyses, and run independently for each set of gene lists. Raw P-values for a given pathway were combined across algorithms using Fisher's method and adjusted for multiple testing corrections by Bonferroni's method. Log 2 transformed fold-change (Log 2FC) was averaged in a similar fashion. A collective significance score proportional to combined p-values and average Log 2FC was generated and scaled from 0-100 to assess the degree of pathway enrichment or depletion relative to the inclusive set.

TABLE 6

EGSEA Gene Set	Adj. P-value	Avg. Log2FC	Direction	Significance
	SNF1			
ALANINE_ASPARTATE_GLUTAMATE_KEGG	6.45E−03	0.3121	+	0.60
AMINO_SUGAR_NUCLEO_METAB_KEGG	5.02E−03	0.2700	−	0.55
ARACHNOID_METAB_KEGG	2.09E−36	0.4538	−	14.32
CASPASE_BIOCARTA	9.64E−01	0.2310	+	0.00
CELL_CYCLE_BIOCARTA	1.14E−08	0.4261	+	2.99
CELL_CYCLE_PROTEASOME_REACTOME	8.97E−27	0.3090	+	7.12
CETUXIMAB_BENEFIT	5.24E−08	1.0630	+	6.84
COMPLEMENT_BIOCARTA	4.85E−33	0.5989	−	17.12
COMPLEMENT_COAG_KEGG	1.45E−104	0.5228	−	48.01

TABLE 6-continued

EGSEA Gene Set	Adj. P-value	Avg. Log2FC	Direction	Significance
CRYPT_BASE	1.46E–30	0.4270	+	11.27
CRYPT_TOP	1.49E–08	0.2952	–	2.04
CSC_BATLLE	4.74E–10	0.3773	–	3.11
EMT_CORE_GENES	3.74E–24	0.7653	–	15.86
EPITH_LOBODA	9.90E–01	0.2649	–	0.00
FATTY_ACID_METAB_KEGG	7.84E–01	0.1922	+	0.02
FGF_ACT_CP	8.71E–02	0.2797	–	0.26
FOLFIRI_RESPONSE	4.09E–06	0.3726	–	1.78
FOLFOX_RESPONSE_DOWN	2.29E–08	0.3564	–	2.41
FRUTOSE_MANNOSE_METAB_KEGG	9.90E–01	0.2460	+	0.00
GALACTOSE_METAB_KEGG	8.80E–01	0.2329	–	0.01
GLUTAMINE_AMINO_ACID_GO_BP	1.48E–01	0.2342	+	0.17
GLUTAMINE_GO_BP	3.09E–12	0.3239	+	3.30
GLUTATHIONE_KEGG	1.49E–01	0.2809	–	0.20
GLYCEROPHOSPHOLIPID_GO_BP	9.90E–01	0.2072	–	0.00
GLYCEROPHOSPHOLIPID_METAB_KEGG	9.64E–01	0.2738	–	0.00
IGF1R_CP	2.73E–01	0.1866	+	0.09
IMMUNE_CD8MACRO_GALON	6.33E–03	0.6922	–	1.35
IMMUNE_ESTIMATE	1.02E–97	0.6903	–	59.21
IMMUNE_MDSC_ALBELDA	2.47E–06	0.3828	–	1.90
IMMUNE_MDSC_CERWENKA	1.85E–08	1.0274	–	7.03
IMMUNE_MSC	3.10E–06	0.4365	–	2.13
IMMUNE_NKC_BREAST	1.03E–10	0.7383	–	6.52
IMMUNE_RESP_GO_BP	4.76E–95	0.5717	–	47.69
IMMUNE_TH1_GALON	1.52E–04	0.5974	–	2.02
IMMUNE_TH17_GOUNARI	2.92E–17	0.4639	–	6.78
IMMUNE_THF_BREAST	8.54E–07	0.5775	–	3.10
IMMUNE_TREG_GALON	6.08E–11	0.7164	–	6.47
IMMUNE_TREG_LUCAS	3.35E–06	0.4439	+	2.15
IMMUNE_TREG_PASTILLE	8.13E–11	0.5885	–	5.25
INTEGRIN_BETA3_CP	1.10E–21	0.4985	–	9.24
INTEGRIN_BIOCARTA	2.26E–03	0.1980	–	0.46
JAK_STAT_GO_BP	1.56E–04	0.3703	–	1.25
JAK_STAT_KEGG	1.94E–13	0.3674	–	4.13
KEGG_CELL_CYCLE	2.88E–22	0.3461	+	6.59
KRAS_50_UP	2.42E–41	0.6080	–	21.84
LINOLEIC_METAB_KEGG	2.12E–24	0.4010	–	8.40
LYSOPHOSPHOLIPID_PID	3.43E–08	0.2692	–	1.78
MAPK_ACT_GO_BP	2.97E–05	0.3023	–	1.21
MAPK_KEGG	3.63E–09	0.3242	–	2.42
MATRIX_REMODEL_REACTOME	4.51E–95	0.5268	–	43.96
MESENCH_LOBODA	8.97E–27	0.5880	–	13.55
MYC_TARGETS_CP	1.43E–24	0.2934	+	6.19
MYC_TARGETS_ZELLER	6.04E–26	0.3278	+	7.31
NFKB_BIOCARTA	1.16E–07	0.2644	–	1.62
NITROGEN_METAB_KEGG	1.52E–02	0.2839	+	0.46
NOTCH_CP	8.55E–01	0.2300	+	0.01
NOTCH_REACTOME	2.85E–01	0.2365	+	0.11
NUCLEOTIDE_METAB_REACTOME	3.43E–08	0.2753	+	1.82
OXALIPLATIN_NCI60	6.42E–06	0.3554	–	1.63
PD1_REACTOME	7.10E–28	0.7587	–	18.22
PENTOSE_GLUC_METAB_KEGG	3.09E–12	0.3239	+	3.30
PI3K_ACT_GO_BP	9.90E–01	0.1734	–	0.00
PI3K_ACT_REACTOME	9.90E–01	0.1734	–	0.00
PROTEASOME_KEGG	1.25E–14	0.1688	+	2.08
SERRATED_UP	1.15E–01	0.2394	+	0.20
SHH_CP	2.99E–01	0.2535	+	0.12
SHH_KEGG	4.90E–22	0.4518	–	8.51
SRC_ACT_BILD	1.07E–01	0.2457	+	0.21
SRC_ACT_BIOCARTA	3.77E–12	0.3583	+	3.62
STARCH_SUCROSE_METAB_KEGG	1.71E–16	0.3235	+	4.51
STROMAL_ESTIMATE	9.72E–148	0.7691	–	100.00
TGFB_1	2.61E–10	0.4074	–	3.45
TGFB_2	5.95E–24	0.3303	–	6.78
TGFB_CORE_GENES	2.26E–01	0.2601	–	0.15
TGFB_KEGG	8.42E–02	0.3318	+	0.31
TRANSLATION_RIBOS_REACTOME	1.48E–18	0.2379	+	3.75
TYROSINE_METAB_KEGG	1.10E–08	0.2592	+	1.82
VEGF_VEGFR_CP	3.57E–07	0.3919	–	2.23

TABLE 6-continued

EGSEA Gene Set	Adj. P-value	Avg. Log2FC	Direction	Significance
VEGF_VEGFR_REACTOME	4.11E−12	0.4352	−	4.38
WNT_BIOCARTA	5.10E−01	0.2460	+	0.06
WNT_FLIER	5.31E−13	0.2419	+	2.63
WOUND_RESPONSE_GO_BP	3.06E−88	0.5037	−	38.98
	SNF2			
ALANINE_ASPARTATE_GLUTAMATE_KEGG	1.43E−03	0.5259	+	2.95
AMINO_SUGAR_NUCLEO_METAB_KEGG	5.45E−08	0.3783	+	5.43
ARACHNOID_METAB_KEGG	2.46E−29	0.5189	+	29.34
CASPASE_BIOCARTA	5.36E−03	0.3318	+	1.49
CELL_CYCLE_BIOCARTA	1.10E−01	0.3805	−	0.72
CELL_CYCLE_PROTEASOME_REACTOME	4.56E−11	0.3522	−	7.20
CETUXIMAB_BENEFIT	2.15E−08	1.1102	−	16.82
COMPLEMENT_BIOCARTA	3.20E−32	0.7351	+	45.76
COMPLEMENT_COAG_KEGG	1.11E−85	0.5955	+	100.00
CRYPT_BASE	2.53E−11	0.3928	−	8.23
CRYPT_TOP	2.53E−11	0.4178	+	8.75
CSC_BATLLE	3.13E−05	0.4805	−	4.28
EMT_CORE_GENES	5.87E−01	0.3254	−	0.15
EPITH_LOBODA	3.89E−10	0.5010	+	9.32
FATTY_ACID_METAB_KEGG	7.43E−02	0.4347	+	0.97
FGF_ACT_CP	3.34E−05	0.3901	+	3.45
FOLFIRI_RESPONSE	9.96E−01	0.2410	−	0.00
FOLFOX_RESPONSE_DOWN	3.49E−06	0.5442	+	5.87
FRUTOSE_MANNOSE_METAB_KEGG	3.61E−16	0.4445	+	13.57
GALACTOSE_METAB_KEGG	9.32E−11	0.3527	+	6.99
GLUTAMINE_AMINO_ACID_GO_BP	5.12E−02	0.5102	+	1.30
GLUTAMINE_GO_BP	1.75E−09	0.4108	+	7.11
GLUTATHIONE_KEGG	7.83E−05	0.3774	+	3.06
GLYCEROPHOSPHOLIPID_GO_BP	1.30E−04	0.4457	+	3.42
GLYCEROPHOSPHOLIPID_METAB_KEGG	1.02E−09	0.4612	+	8.19
IGF1R_CP	6.73E−07	0.3664	−	4.47
IMMUNE_CD8MACRO_GALON	3.89E−04	0.7371	+	4.97
IMMUNE_ESTIMATE	1.11E−52	0.5728	+	58.83
IMMUNE_MDSC_ALBELDA	1.41E−07	0.4591	+	6.22
IMMUNE_MDSC_CERWENKA	6.48E−07	0.7856	+	9.61
IMMUNE_MSC	4.72E−31	0.8030	+	48.14
IMMUNE_NKC_BREAST	2.71E−02	0.4827	+	1.49
IMMUNE_RESP_GO_BP	2.59E−62	0.5539	+	67.43
IMMUNE_TH1_GALON	2.81E−12	0.8923	+	20.37
IMMUNE_TH17_GOUNARI	3.57E−03	0.4321	+	2.09
IMMUNE_THF_BREAST	3.49E−06	0.6384	+	6.89
IMMUNE_TREG_GALON	1.46E−09	0.5948	+	10.39
IMMUNE_TREG_LUCAS	9.29E−12	0.4583	−	9.99
IMMUNE_TREG_PASTILLE	8.63E−02	0.2034	+	0.43
INTEGRIN_BETA3_CP	7.41E−06	0.4001	+	4.06
INTEGRIN_BIOCARTA	9.72E−17	0.4216	+	13.34
JAK_STAT_GO_BP	5.83E−03	0.4044	+	1.79
JAK_STAT_KEGG	4.05E−08	0.4469	+	6.53
KEGG_CELL_CYCLE	6.84E−13	0.4137	−	9.95
KRAS_50_UP	5.03E−25	0.5018	+	24.10
LINOLEIC_METAB_KEGG	1.76E−21	0.5265	+	21.60
LYSOPHOSPHOLIPID_PID	5.74E−22	0.4198	+	17.62
MAPK_ACT_GO_BP	2.04E−14	0.4992	+	13.51
MAPK_KEGG	3.38E−09	0.4381	+	7.33
MATRIX_REMODEL_REACTOME	8.79E−52	0.4832	+	48.76
MESENCH_LOBODA	1.82E−01	0.3600	−	0.53
MYC_TARGETS_CP	6.43E−04	0.3331	−	2.10
MYC_TARGETS_ZELLER	3.81E−10	0.3521	−	6.55
NFKB_BIOCARTA	1.36E−17	0.4104	+	13.68
NITROGEN_METAB_KEGG	4.79E−02	0.4037	−	1.05
NOTCH_CP	7.65E−08	0.3734	−	5.25
NOTCH_REACTOME	3.31E−06	0.3412	−	3.70
NUCLEOTIDE_METAB_REACTOME	2.26E−04	0.3892	+	2.80
OXALIPLATIN_NCI60	4.97E−03	0.3641	−	1.66
PD1_REACTOME	7.31E−17	0.5907	+	18.84
PENTOSE_GLUC_METAB_KEGG	1.75E−09	0.4108	+	7.11
PI3K_ACT_GO_BP	4.09E−05	0.3884	+	3.37
PI3K_ACT_REACTOME	4.09E−05	0.3884	+	3.37
PROTEASOME_KEGG	8.41E−08	0.2689	−	3.76
SERRATED_UP	1.57E−08	0.3446	−	5.32
SHH_CP	1.48E−07	0.3289	−	4.44
SHH_KEGG	7.70E−07	0.3720	+	4.49
SRC_ACT_BILD	3.87E−17	0.4149	−	13.46
SRC_ACT_BIOCARTA	9.23E−02	0.3573	+	0.73

TABLE 6-continued

EGSEA Gene Set	Adj. P-value	Avg. Log2FC	Direction	Significance
STARCH_SUCROSE_METAB_KEGG	1.35E−13	0.4711	+	11.98
STROMAL_ESTIMATE	1.81E−55	0.4198	+	45.42
TGFB_1	6.58E−02	0.4142	+	0.97
TGFB_2	5.14E−49	0.4962	+	47.36
TGFB_CORE_GENES	1.22E−07	0.4831	−	6.60
TGFB_KEGG	4.83E−15	0.4436	−	12.55
TRANSLATION_RIBOS_REACTOME	2.67E−09	0.3371	−	5.71
TYROSINE_METAB_KEGG	4.13E−08	0.4382	+	6.40
VEGF_VEGFR_CP	9.96E−01	0.2307	−	0.00
VEGF_VEGFR_REACTOME	9.96E−01	0.2565	−	0.00
WNT_BIOCARTA	3.13E−05	0.3676	+	3.27
WNT_FLIER	4.28E−01	0.3477	−	0.25
WOUND_RESPONSE_GO_BP	1.53E−64	0.5058	+	63.80
ALANINE_ASPARTATE_GLUTAMATE_KEGG	5.38E−08	0.5005	−	4.34
AMINO_SUGAR_NUCLEO_METAB_KEGG	8.96E−04	0.3264	−	1.19
ARACHNOID_METAB_KEGG	5.66E−31	0.4584	−	16.53
CASPASE_BIOCARTA	5.30E−02	0.2693	+	0.41
CELL_CYCLE_BIOCARTA	2.84E−03	0.3496	−	1.06
CELL_CYCLE_PROTEASOME_REACTOME	1.58E−02	0.2808	−	0.60
CETUXIMAB_BENEFIT	1.00E+00	0.1997	−	0.00
COMPLEMENT_BIOCARTA	2.71E−35	0.7185	−	29.61
COMPLEMENT_COAG_KEGG	6.88E−116	0.7284	−	100.00
CRYPT_BASE	7.28E−13	0.4123	−	5.97
CRYPT_TOP	7.38E−10	0.3274	+	3.56
CSC_BATLLE	2.09E−12	0.4522	+	6.30
EMT_CORE_GENES	3.86E−20	0.7973	+	18.45
EPITH_LOBODA	3.04E−10	0.4000	−	4.54
FATTY_ACID_METAB_KEGG	3.41E−03	0.4052	−	1.19
FGF_ACT_CP	8.54E−07	0.4215	−	3.05
FOLFIRI_RESPONSE	1.72E−05	0.4294	+	2.44
FOLFOX_RESPONSE_DOWN	8.63E−11	0.5447	+	6.53
FRUTOSE_MANNOSE_METAB_KEGG	4.90E−17	0.4120	−	8.01
GALACTOSE_METAB_KEGG	3.63E−08	0.3088	−	2.74
GLUTAMINE_AMINO_ACID_GO_BP	6.80E−07	0.5101	−	3.75
GLUTAMINE_GO_BP	8.45E−18	0.4575	−	9.31
GLUTATHIONE_KEGG	3.26E−03	0.2964	−	0.88
GLYCEROPHOSPHOLIPID_GO_BP	8.48E−03	0.3131	−	0.77
GLYCEROPHOSPHOLIPID_METAB_KEGG	3.23E−08	0.3738	−	3.34
IGF1R_CP	4.19E−04	0.2910	+	1.17
IMMUNE_CD8MACRO_GALON	1.00E+00	0.3206	+	0.00
IMMUNE_ESTIMATE	4.75E−31	0.4060	+	14.68
IMMUNE_MDSC_ALBELDA	8.41E−05	0.3353	−	1.63
IMMUNE_MDSC_CERWENKA	1.00E+00	0.3405	+	0.00
IMMUNE_MSC	4.59E−13	0.3666	−	5.39
IMMUNE_NKC_BREAST	2.42E−01	0.2869	+	0.21
IMMUNE_RESP_GO_BP	9.88E−59	0.4223	+	29.20
IMMUNE_TH1_GALON	6.41E−01	0.2950	−	0.07
IMMUNE_TH17_GOUNARI	5.66E−06	0.4089	+	2.56
IMMUNE_THF_BREAST	1.00E+00	0.3467	+	0.00
IMMUNE_TREG_GALON	1.00E+00	0.2405	−	0.00
IMMUNE_TREG_LUCAS	2.31E−07	0.4439	+	3.51
IMMUNE_TREG_PASTILLE	5.74E−02	0.4276	+	0.63
INTEGRIN_BETA3_CP	1.06E−13	0.4956	+	7.67
INTEGRIN_BIOCARTA	2.22E−08	0.3730	−	3.40
JAK_STAT_GO_BP	7.54E−01	0.3675	−	0.05
JAK_STAT_KEGG	4.76E−02	0.3342	+	0.53
KEGG_CELL_CYCLE	8.88E−02	0.3310	−	0.41
KRAS_50_UP	1.79E−44	0.6332	+	33.02
LINOLEIC_METAB_KEGG	8.13E−33	0.4636	−	17.73
LYSOPHOSPHOLIPID_PID	5.74E−04	0.3199	−	1.24
MAPK_ACT_GO_BP	2.43E−05	0.4404	−	2.42
MAPK_KEGG	2.11E−10	0.3684	+	4.25
MATRIX_REMODEL_REACTOME	1.01E−61	0.4717	+	34.30
MESENCH_LOBODA	3.07E−29	0.6368	+	21.64
MYC_TARGETS_CP	8.11E−09	0.3002	−	2.90
MYC_TARGETS_ZELLER	1.24E−02	0.2744	−	0.62
NFKB_BIOCARTA	6.61E−03	0.2917	−	0.76
NITROGEN_METAB_KEGG	1.36E−03	0.4234	+	1.45
NOTCH_CP	4.29E−05	0.2752	+	1.43
NOTCH_REACTOME	3.76E−06	0.3093	+	2.00
NUCLEOTIDE_METAB_REACTOME	2.11E−10	0.3340	−	3.85
OXALIPLATIN_NCI60	5.48E−06	0.3886	+	2.44
PD1_REACTOME	1.00E−04	0.3976	+	1.90
PENTOSE_GLUC_METAB_KEGG	8.45E−18	0.4575	−	9.31
PI3K_ACT_GO_BP	1.38E−05	0.3182	−	1.84

TABLE 6-continued

EGSEA Gene Set	Adj. P-value	Avg. Log2FC	Direction	Significance
PI3K_ACT_REACTOME	1.38E−05	0.3182	–	1.84
PROTEASOME_KEGG	1.48E−02	0.2122	–	0.46
SERRATED_UP	1.16E−16	0.3067	+	5.83
SHH_CP	3.58E−03	0.2572	–	0.75
SHH_KEGG	1.24E−11	0.3951	+	5.14
SRC_ACT_BILD	9.94E−14	0.3454	+	5.35
SRC_ACT_BIOCARTA	5.14E−15	0.4159	–	7.08
STARCH_SUCROSE_METAB_KEGG	3.00E−24	0.4139	–	11.61
STROMAL_ESTIMATE	9.00E−122	0.6830	+	98.55
TGFB_1	1.64E−04	0.4405	+	1.99
TGFB_2	1.44E−09	0.2866	–	3.02
TGFB_CORE_GENES	1.03E−13	0.4248	+	6.58
TGFB_KEGG	1.35E−21	0.4521	+	11.25
TRANSLATION_RIBOS_REACTOME	6.09E−01	0.2140	+	0.05
TYROSINE_METAB_KEGG	8.03E−17	0.4869	–	9.34
VEGF_VEGFR_CP	4.29E−05	0.3031	+	1.58
VEGF_VEGFR_REACTOME	6.99E−11	0.3939	+	4.77
WNT_BIOCARTA	8.48E−03	0.2987	–	0.74
WNT_FLIER	2.87E−13	0.3158	–	4.72
WOUND_RESPONSE_GO_BP	8.75E−83	0.5050	+	49.40

[0126] Table 7: Immune genes over-expressed in SNF2 metastases. Immune genes were extracted from the Hallmark signatures 'inflammatory response', 'interferon alpha response', and 'interferon gamma response', in addition to the custom gene sets 'immune estimate', 'immune msc', 'immune response', and 'immune Th1'. Shown are differentially expressed genes in the comparison of SNF2 metastases to SNF1 and 3 metastases. Fold-change denotes ratio of SNF2 vs. SNF1+SNF3. P-value corrected for multiple comparisons using the Benjamini-Hochberg method.

TABLE 7

Entrez ID	Gene Symbol	log2FC	adj P-Value
101	ADAM8	1.114151605	0.001613248
116071	BATF2	1.050030827	0.000402744
684	BST2	1.447305503	7.0543E−05
6352	CCL5	1.330458386	0.007095402
929	CD14	1.130725029	0.012587909
924	CD7	1.267542763	0.032153144
3732	CD82	1.023562283	3.13456E−05
10164	CHST4	1.337259457	0.010577936
129607	CMPK2	1.267895875	0.00020464
11151	CORO1A	1.197059439	0.003971877
1439	CSF2RB	1.217270252	0.000537403
1441	CSF3R	1.135318253	0.004176407
1521	CTSW	1.284888258	0.033477783
6373	CXCL11	1.316957277	0.003212995
10148	EBI3	1.096193201	0.033105492
10578	GNLY	1.493818884	0.004665499
85441	HELZ2	1.03828577	0.000280215
3106	HLA-B	1.146355659	0.000498987
3107	HLA-C	1.021905249	0.000106004
3134	HLA-F	1.48934274	7.63496E−05
3135	HLA-G	1.426661079	0.016403862
3620	IDO1	1.574024748	0.018152649
2537	IFI6	1.29363079	0.00273504
3560	IL2RB	1.211399747	0.004000797
3665	IRF7	1.127754457	7.13225E−05
9636	ISG15	1.482687141	0.000641825
3695	ITGB7	1.027118954	0.000731855
3965	LGALS9	1.086883884	8.64875E−05
10859	LILRB1	1.04319418	0.002360525
10288	LILRB2	1.093481863	0.006651359
4050	LTB	1.391843525	0.0077572
4210	MEFV	1.50658012	0.000626788
931	MS4A1	1.597053128	0.014568052
4599	MX1	1.133975285	0.005273497
4689	NCF4	1.013940329	0.00594171
150372	NFAM1	1.022460225	0.000668619

TABLE 7-continued

Entrez ID	Gene Symbol	log2FC	adj P-Value
4818	NKG7	1.845375061	0.001205486
84166	NLRC5	1.378670195	0.000117444
4939	OAS2	1.18680124	0.003515069
8638	OASL	1.264199434	0.000440086
5133	PDCD1	1.674556616	0.001721488
23533	PIK3R5	1.013268448	0.0057499
5551	PRF1	1.166608919	0.032817116
5699	PSMB10	1.034307259	1.21519E−05
5698	PSMB9	1.002183641	0.000622372
9051	PSTPIP1	1.096234149	0.012609516
8698	S1PR4	1.296702606	0.01465708
8578	SCARF1	1.169639656	2.27411E−05
6398	SECTM1	1.201216841	0.001565863
8651	SOCS1	1.111619994	0.010405385
23166	STAB1	1.006190485	0.001542236
6890	TAP1	1.115449843	0.000228619
10312	TCIRG1	1.191293713	2.12027E−05
7127	TNFAIP2	1.024200168	0.003936091
8744	TNFSF9	1.289096356	0.011517123
11274	USP18	1.332873246	0.000168582
7454	WAS	1.080728587	0.003571432
54739	XAF1	1.199077362	0.000854797
7535	ZAP70	1.1775269	0.026150135
81030	ZBP1	1.81033816	1.47166E−05

[0127] Table 8: Significantly mutated genes determined by MutSigCV. All variants that passed validation criteria in coding regions were categorized and tabulated to create an overall mutation type summary for each gene. n_syn=number of synonymous mutations; n_mis=number of missense mutations; n_lof=number of loss-of-function mutations; n_splice=number of splice junction mutations; n_indels_mis=number of inserts/deletions causing missense mutations; n_indels_lof=number of insertions/deletions causing loss-of-function mutations; num_unique=number of unique instances of a point mutation seen. MutSigCV v1.2 determined the probability of base level mutations within specific gene-level contexts given overall mutation rate, ratio of synonymous to non-synonymous mutation types, and other gene-levels factors including estimates of expression, replication rate, and chromatin state[21]. Raw P-values indicate the probability that the number of somatic mutations found within each gene is observed by chance with multiple testing corrections controlled by false discovery rate (FDR, q-value).

TABLE 8

Gene name	n_syn	n_mis	n_non	n_lof	n_splice	n_indels_mis	n_indels_lof	num_ unique	P-value	FDR (q-value)
KRAS	0	22	0	0	0	0	0	4	0	0
APC	1	11	0	49	4	0	22	59	2.7E−15	2.5E−11
TP53	0	32	0	7	0	1	6	32	4.2E−15	2.7E−11
PIK3CA	0	20	0	0	0	0	0	14	6.6E−09	3.1E−05
FBXW7	0	7	0	2	0	0	0	9	4.5E−06	0.01681
SOX9	0	0	0	3	0	1	4	7	6E−06	0.01889
SMAD4	0	6	0	1	0	0	1	7	9.3E−06	0.02503
NPPB	0	3	0	0	0	0	0	3	0.00012	0.27423
NRAS	0	4	0	0	0	0	0	4	0.0002	0.4191
TSC1	0	1	0	0	0	12	1	3	0.00033	0.62637
RPL22	0	2	0	0	0	0	0	2	0.00052	0.88454
KDR	0	6	0	1	0	4	0	9	0.00061	0.95729
HIST1H3I	0	0	0	2	0	0	0	2	0.00094	1
THSD7A	0	8	0	0	0	0	0	8	0.00233	1
CTNNA2	0	6	0	0	1	0	0	7	0.00269	1
RNF2	0	2	0	1	0	0	0	3	0.00283	1
RASA1	0	3	0	1	0	0	0	4	0.00496	1
NUF2	0	3	0	0	0	0	0	3	0.00609	1
CYP1A2	0	3	0	0	0	0	0	3	0.00612	1
GPHN	0	4	0	0	0	0	0	2	0.00717	1
SOX10	0	3	0	0	0	0	0	3	0.0075	1
CSMD3	4	20	0	1	1	0	1	27	0.00752	1
TWSG1	0	2	0	0	0	0	0	2	0.00888	1
NPM1	0	2	0	0	0	0	0	2	0.01038	1
PAX3	0	4	0	0	0	0	0	4	0.01063	1
RUNX1T1	0	5	0	3	0	0	0	7	0.0109	1
FGF23	0	3	0	0	0	0	0	3	0.01166	1
ESR1	0	5	0	0	0	0	0	4	0.01176	1
RPN1	0	3	0	0	0	0	0	3	0.01194	1
GNA13	1	2	0	1	0	0	0	4	0.01337	1
SHCBP1	0	2	0	0	0	0	0	2	0.01427	1
SOCS1	0	2	0	0	0	0	0	2	0.01553	1
EZH2	0	5	0	0	0	0	0	5	0.0168	1
SLCO1B1	0	2	0	0	0	0	0	2	0.01973	1
FLG	5	12	0	1	0	0	0	18	0.01985	1
HIST1H1E	1	2	0	0	0	0	0	3	0.02062	1
PTEN	0	2	0	1	0	0	0	3	0.02155	1
SPATA17	0	1	0	1	0	0	0	2	0.02215	1
CHN1	0	1	0	0	0	1	0	2	0.02263	1
CDK12	0	3	0	0	0	0	1	4	0.02268	1
EBF1	0	5	0	0	0	0	0	4	0.02279	1
ARID2	0	4	0	1	0	0	0	5	0.02333	1
SMAD3	0	3	0	0	0	0	0	3	0.02338	1
MTRR	0	3	0	0	0	0	1	4	0.02339	1
EPHB1	0	4	0	0	0	0	1	4	0.02451	1
BLID	0	1	0	0	0	0	0	4	0.0249	1
EP300	0	3	0	2	0	0	2	7	0.02613	1
CDH11	0	5	0	0	0	0	0	5	0.02635	1
BRIP1	0	4	0	0	0	0	0	4	0.02771	1
SLC2A1	0	2	0	0	0	0	0	2	0.02786	1
TP63	2	4	0	0	1	0	0	7	0.02843	1
CCDC6	0	2	0	0	0	0	0	2	0.02905	1
WT1	0	2	0	0	0	0	0	2	0.02993	1
NAA16	0	2	0	0	0	0	1	3	0.03071	1
PTGIS	0	2	0	0	0	0	0	2	0.03085	1
BCL11B	0	4	0	0	0	0	0	4	0.03422	1
H3F3B	0	1	0	0	0	0	0	1	0.03444	1
ANKRD37	0	1	0	0	0	0	0	1	0.03466	1
FKBP1B	0	1	0	0	0	0	0	1	0.0368	1
NHP2	0	2	0	0	0	0	0	2	0.03717	1
CYP2A6	0	2	0	0	0	0	0	2	0.03817	1
INHBA	0	3	0	0	0	0	0	3	0.03889	1
ZNF331	0	5	0	0	0	0	0	5	0.04057	1
SEMA3E	1	4	0	0	1	0	0	6	0.04147	1
HK2	2	2	0	2	0	0	0	5	0.0445	1
PRSS1	0	1	0	0	0	0	0	1	0.04514	1
NUDT3	0	1	0	0	0	0	0	1	0.04532	1
LRP1B	6	20	0	3	3	1	3	33	0.0471	1
VTI1A	0	0	0	1	0	0	0	1	0.0474	1

TABLE 8-continued

Gene name	n_syn	n_mis	n_non	n_lof	n_splice	n_indels_mis	n_indels_lof	num_ unique	P-value	FDR (q-value)
HIST1H3B	0	1	0	0	0	0	0	1	0.04747	1
DOCK2	1	7	0	1	0	0	1	10	0.04843	1
TCF7L2	0	2	0	6	1	0	2	11	0.04894	1
WDR48	0	4	0	1	0	0	0	4	0.05144	1
FGFR1OP2	0	0	0	1	0	0	0	1	0.05201	1
BUB1B	1	4	0	0	0	0	0	5	0.05216	1
ACVR2A	0	1	0	2	0	0	1	4	0.05637	1
ZIM2	1	3	0	0	0	0	0	4	0.05666	1
KLHL6	1	3	0	0	0	0	0	4	0.05694	1
PPP2R1A	0	1	0	1	0	0	0	2	0.0601	1
INSL6	0	0	0	1	0	0	0	1	0.06116	1
RPS10	0	0	0	1	0	0	0	1	0.06116	1
JAZF1	0	2	0	0	0	0	0	2	0.06237	1
MARK1	1	3	0	0	0	0	0	4	0.06297	1
CYLD	0	3	0	0	1	0	0	4	0.06322	1
GALNT12	0	2	0	0	0	0	0	2	0.06372	1
FMN2	1	4	0	1	0	1	0	7	0.06374	1
TAF12	0	1	0	0	0	0	0	1	0.06397	1
SPINK1	0	1	0	0	0	0	0	1	0.06432	1
CTCF	0	2	0	0	0	0	1	3	0.06449	1
MAP3K7	1	2	0	0	0	0	0	3	0.06524	1
FOXR2	0	1	0	0	0	0	0	1	0.06525	1
NCOA4	0	2	0	0	0	0	0	2	0.06567	1
XRCC5	0	2	0	0	0	0	0	2	0.07085	1
TRAF5	0	3	0	0	0	0	0	3	0.07149	1
BRAF	0	3	0	0	0	0	0	2	0.07164	1
ABCD2	0	5	0	0	0	0	0	5	0.07337	1
CREB1	0	1	0	0	0	0	0	1	0.0746	1
GREM1	0	1	0	0	0	0	0	1	0.07752	1
SLC6A2	1	3	0	0	1	0	0	5	0.07753	1
IRS2	0	6	0	0	0	2	0	7	0.07766	1
DIS3L2	0	2	0	0	0	1	0	3	0.07784	1
HSD17B7	0	1	0	0	0	0	0	1	0.07817	1
RAF1	0	3	0	0	0	0	0	3	0.07861	1
LPHN3	3	8	0	0	1	0	0	11	0.07872	1
WDR36	0	2	0	0	0	0	1	3	0.07921	1
PRKAR1A	0	1	0	1	0	0	0	2	0.08113	1
CSF3R	0	1	0	1	0	0	0	2	0.08358	1
MAGEA1	0	1	0	0	0	0	0	1	0.085381	1
OPTN	0	1	0	1	0	0	0	2	0.08753	1
KLK2	0	0	0	1	0	0	0	1	0.08783	1
THRAP3	1	2	0	0	0	0	0	3	0.08945	1
DRD1	0	1	0	0	0	0	0	1	0.08951	1
TFG	0	2	0	0	0	0	0	2	0.08966	1
B2M	0	0	0	0	0	0	1	1	0.09012	1
C11orf30	0	3	0	0	0	0	0	3	0.09037	1
CSF1R	1	3	0	0	0	0	0	3	0.09085	1
CDH10	0	5	0	0	0	0	0	5	0.09135	1
RALGDS	0	1	0	1	0	0	0	2	0.09284	1
HOXA3	0	1	0	0	0	0	0	1	0.09611	1
PXDN	4	7	0	0	0	0	0	10	0.09621	1
CYP2C18	0	1	0	0	0	0	0	1	0.09824	1
PRDM9	3	5	0	1	0	0	0	9	0.10326	1
ITGA10	0	2	0	0	0	0	0	2	0.10338	1
DNMT3A	0	3	0	0	0	0	1	4	0.10375	1
LPP	0	2	0	0	0	0	0	2	0.10832	1
SEMA3A	0	2	0	0	0	0	0	2	0.11036	1
LTF	1	3	0	0	0	0	0	4	0.11134	1
MSI2	0	1	0	0	0	0	0	1	0.11245	1
MAP2K4	1	1	0	0	0	0	0	2	0.11325	1
ZNF320	0	1	0	0	0	0	0	1	0.11338	1
CSMD1	3	8	0	0	2	0	1	14	0.11491	1
IL7R	0	2	0	0	0	0	0	2	0.11984	1
APOA1	0	1	0	0	0	0	0	1	0.12055	1
CLTCL1	2	4	0	0	0	0	1	7	0.12229	1
CCDC141	1	1	0	1	0	0	0	3	0.12235	1
GOPC	0	2	0	0	0	0	0	2	0.12248	1
CXCR4	0	2	0	0	0	0	0	2	0.12339	1
DNAH5	5	17	0	0	0	0	0	21	0.12421	1
HOXD11	0	0	0	1	0	0	0	1	0.12442	1
ABCG1	1	3	0	0	0	0	0	4	0.12739	1
PTPN11	0	1	0	1	0	0	0	2	0.12857	1
CA9	0	1	0	1	0	0	0	2	0.13143	1
JAK1	0	2	0	0	0	0	0	2	0.13246	1

TABLE 8-continued

Gene name	n_syn	n_mis	n_non	n_lof	n_splice	n_indels_mis	n_indels_lof	num_ unique	P-value	FDR (q-value)
ANTXR2	0	1	0	0	0	0	0	1	0.13305	1
IKZF2	0	2	0	0	0	0	0	2	0.13412	1
HIST1H4L	0	1	0	0	0	0	0	1	0.13416	1
KTN1	1	7	0	0	0	0	0	8	0.13604	1
TAF1L	2	3	0	1	0	0	0	6	0.13611	1
SEC31A	1	2	0	2	0	0	0	5	0.13624	1
RPS7	0	1	0	0	0	0	0	1	0.13632	1
CCL19	0	1	0	0	0	0	0	1	0.13742	1
SLC38A6	0	1	0	0	1	0	0	2	0.13873	1
GALNT3	0	0	0	1	0	0	0	1	0.13897	1
HIST1H4F	0	1	0	0	0	0	0	1	0.14096	1
GLCCI1	0	1	0	0	0	0	0	1	0.14392	1
FKBP5	0	2	0	0	0	0	0	2	0.14538	1
ABCB1	0	5	0	0	0	0	0	5	0.14569	1
PRSS37	0	1	0	0	1	0	0	2	0.14599	1
FKBP9	0	1	0	0	0	0	0	1	0.14717	1
SLC16A4	0	1	0	0	0	0	0	1	0.14736	1
AFF1	0	3	0	1	0	0	0	3	0.14938	1
RAD50	1	0	4	0	1	0	0	6	0.15015	1
MAOA	0	1	0	0	0	0	0	1	0.15035	1
ROBO3	0	3	0	0	0	0	0	3	0.15035	1
STAT4	0	2	0	0	0	0	0	2	0.15171	1
CRBN	0	2	0	0	0	0	0	2	0.15429	1
ARID4A	1	4	0	1	0	0	0	6	0.15491	1
CYP2R1	0	2	0	1	0	0	0	3	0.15702	1
CCDC63	0	2	0	0	0	0	0	2	0.16057	1
IKZF3	0	2	0	0	0	0	0	2	0.16228	1
PSIP1	0	1	0	0	0	0	0	1	0.16432	1
ZNF490	1	1	0	0	0	0	0	2	0.16512	1
CASP8	1	1	0	0	0	0	0	2	0.16541	1
PAK7	0	3	0	0	0	0	0	3	0.16639	1
NCOA3	0	2	0	0	0	0	0	2	0.16712	1
MCCC1	0	1	0	0	0	0	0	1	0.169	1
CD58	0	1	0	0	0	0	0	1	0.1694	1
SUZ12	0	2	0	0	0	0	0	2	0.17011	1
FRMPD1	0	4	0	0	0	0	0	4	0.1715	1
GATA3	0	1	0	0	0	1	0	2	0.17195	1
IL11	0	1	0	0	0	0	0	1	0.17335	1
HIST1H3C	0	1	0	0	0	0	0	1	0.17367	1
ETV4	0	1	0	0	0	0	0	1	0.17572	1
GATA2	0	1	0	0	0	0	0	1	0.17574	1
HOXA9	0	1	0	0	0	0	0	1	0.17645	1
SRC	0	2	0	0	0	0	0	2	0.17816	1
GPC3	0	2	0	0	0	0	0	2	0.18009	1
NPAT	0	3	0	1	0	0	0	4	0.18105	1
SGK1	0	1	0	0	0	0	0	1	0.18136	1
SHOC2	1	2	0	0	0	0	0	3	0.18329	1
HSP90AB1	0	1	0	0	0	0	0	1	0.18408	1
TGM7	0	2	0	0	0	0	0	2	0.18587	1
EXO1	0	4	0	0	0	0	0	4	0.18695	1
LTBP3	0	2	0	0	0	0	0	2	0.18713	1
POT1	0	2	0	0	0	0	1	3	0.18791	1
ROBO1	0	0	0	3	0	8	0	6	0.18853	1
BCHE	0	5	0	1	0	0	0	6	0.1903	1
ARAF	0	3	0	0	0	0	0	3	0.19112	1
PIK3R1	0	3	0	2	0	1	0	6	0.19139	1
CSF1	1	2	0	0	0	0	0	3	0.19189	1
PSRC1	0	1	0	0	0	0	0	1	0.19209	1
NR4A3	0	3	0	0	0	0	1	4	0.19487	1
ARHGAP21	1	4	0	0	0	0	0	5	0.1949	1
RRAGD	0	1	0	0	0	0	0	1	0.19513	1
PDCD1	0	1	0	0	0	0	0	1	0.19608	1
SETBP1	1	6	0	0	0	0	0	7	0.19978	1
RUNX1	0	2	0	0	0	0	0	2	0.2	1
FANCC	0	3	0	0	0	0	0	3	0.20029	1
DNMT3B	0	1	0	0	0	0	0	1	0.20041	1
PCDHGA2	0	2	0	0	0	0	0	2	0.201	1
COMT	0	0	0	1	0	0	0	1	0.201	1
ZFHX4	3	14	0	1	2	0	0	20	0.20245	1
FAS	0	1	0	0	0	0	0	1	0.20374	1
RPS6KA2	0	1	0	1	1	0	0	3	0.20474	1
TBXAS1	1	2	0	0	0	0	0	3	0.20486	1
NTF3	0	0	0	1	0	0	0	1	0.20536	1
FOXP1	0	1	0	1	0	0	0	2	0.20581	1

TABLE 8-continued

Gene name	n_syn	n_mis	n_non	n_lof	n_splice	n_indels_mis	n_indels_lof	num_ unique	P-value	FDR (q-value)
NT5C2	0	2	0	0	0	0	0	2	0.20613	1
CACNA1S	1	3	0	0	0	1	0	5	0.20628	1
SOS1	0	2	0	0	0	0	0	2	0.2069	1
CHEK2	0	0	0	1	1	0	0	2	0.20824	1
TOP1	0	1	0	0	2	0	0	3	0.20871	1
NLRP7	1	3	0	0	0	1	0	5	0.20892	1
HMCN1	1	15	0	3	1	0	0	19	0.2094	1
FOXO3	1	0	0	0	0	0	1	2	0.21008	1
NUP98	0	3	0	0	0	0	0	3	0.21024	1
INPP4B	0	1	0	0	0	0	0	1	0.21038	1
SMUG1	0	1	0	0	0	0	0	1	0.21123	1
TLR4	1	2	0	0	0	0	0	3	0.21202	1
CDK4	0	0	0	1	0	0	0	1	0.21245	1
AKT3	0	1	0	0	0	0	0	1	0.21261	1
PLK2	0	2	0	0	0	0	0	2	0.21301	1
CYP2C8	0	0	0	0	0	1	0	1	0.21387	1
MTUS2	1	3	0	0	0	0	0	4	0.21493	1
SLC47A2	0	0	0	1	0	0	0	1	0.21662	1
PTPN3	0	2	0	0	0	0	0	2	0.21787	1
MBD4	0	1	0	0	0	0	0	1	0.2181	1
NTRK2	0	3	0	0	0	0	0	3	0.21818	1
DDX10	0	2	0	0	0	0	0	2	0.21848	1
SFRP1	0	1	0	0	0	0	0	1	0.21877	1
MYB	1	1	0	0	0	0	0	2	0.2192	1
PTHLH	0	1	0	0	0	0	0	1	0.2192	1
FGFR1OP	0	1	0	0	1	0	0	2	0.21955	1
K1AA1524	0	0	0	1	0	0	0	1	0.22331	1
STAT6	0	1	0	0	0	0	0	1	0.22534	1
SLC22A1	1	1	0	0	0	0	0	2	0.22599	1
EPCAM	0	0	0	1	0	0	0	1	0.22776	1
CIITA	0	2	0	0	0	0	0	2	0.22896	1
FGF3	0	1	0	0	0	0	0	1	0.23035	1
IDH1	0	1	0	0	0	0	0	1	0.23269	1
ICAM2	0	1	0	0	0	0	0	1	0.23291	1
PSMA7	0	1	0	0	0	0	0	1	0.23321	1
AFF2	2	4	0	0	0	0	0	6	0.23403	1
EPAS1	0	1	0	0	0	0	0	1	0.23407	1
UACA	0	2	0	0	0	1	0	3	0.23507	1
HIF1A	0	1	0	1	0	0	0	2	0.2352	1
MYSM1	0	1	0	0	0	0	0	1	0.23523	1
CCND2	0	1	0	0	0	0	0	1	0.23837	1
HTR1A	0	2	0	0	0	0	0	2	0.23906	1
MAX	0	1	0	0	0	0	0	1	0.23933	1
AXIN1	0	1	0	0	0	0	1	2	0.24218	1
HOXB13	0	1	0	0	0	0	0	1	0.24487	1
TRIM33	0	1	0	0	1	0	0	2	0.24518	1
CIC	2	2	0	0	0	0	0	4	0.2461	1
CD79A	0	1	0	0	0	0	0	1	0.24766	1
YWHAE	0	1	0	0	0	0	0	1	0.25035	1
MSH6	0	8	0	0	0	0	0	6	0.24092	1
HMGCR	1	3	0	0	0	0	0	4	0.25093	1
STX11	0	1	0	0	0	0	0	1	0.25323	1
SLCO1A2	0	1	0	0	0	0	0	1	0.25335	1
FCGR2B	0	0	0	1	0	0	0	1	0.25434	1
ABCA12	4	8	0	1	2	0	0	15	0.25652	1
NDC80	0	1	0	0	0	0	0	1	0.25729	1
AURKC	0	1	0	0	0	0	0	1	0.25786	1
PAX6	0	1	0	0	0	0	0	1	0.25849	1
CEP57	0	1	0	0	0	0	0	1	0.261	1
PRKDC	1	7	0	1	4	0	0	13	0.2615	1
PIK3CB	0	2	0	0	0	0	0	2	0.26338	1
SMARCB1	0	1	0	0	0	0	0	1	0.27128	1
EAF2	0	0	0	1	0	0	0	1	0.27185	1
CREB3L1	1	0	0	1	0	0	0	2	0.27399	1
NTRK3	1	3	0	0	0	0	0	4	0.27585	1
CASR	0	2	0	0	0	0	0	2	0.27702	1
ERBB2	0	3	0	0	0	0	0	3	0.28052	1
RIMS2	1	10	0	0	0	0	0	11	0.28099	1
PRDM1	1	2	0	0	1	0	0	4	0.28236	1
CLTC	1	2	0	0	0	0	0	3	0.28258	1
ETV5	0	1	0	0	0	0	0	1	0.28279	1
CDH1	1	4	0	0	0	0	0	5	0.2839	1
NFKB1	1	2	0	0	0	0	0	3	0.28581	1
IKBKB	0	1	0	0	0	0	0	1	0.28589	1

TABLE 8-continued

Gene name	n_syn	n_mis	n_non	n_lof	n_splice	n_indels_mis	n_indels_lof	num_ unique	P-value	FDR (q-value)
CAMTA1	0	2	0	0	0	0	0	2	0.28901	1
ZNF384	0	1	0	0	0	0	0	1	0.28973	1
TGFBR2	1	0	0	1	0	0	2	3	0.28993	1
MSH3	0	2	0	0	0	1	0	3	0.29008	1
ATP2B3	0	3	0	0	0	0	0	3	0.2912	1
ACSL6	1	1	0	0	0	0	0	2	0.29274	1
UGT1A1	0	1	0	0	0	0	0	1	0.29277	1
PALB2	1	1	0	0	0	0	1	3	0.29307	1
ITGB3	0	2	0	0	0	0	0	2	0.29406	1
BCORL1	0	2	0	0	0	0	0	2	0.29488	1
PCDH15	0	8	0	1	1	0	0	10	0.29552	1
STAT3	0	1	0	0	0	0	0	1	0.29587	1
MAML2	1	3	0	0	0	0	0	4	0.29652	1
BCL9	1	1	0	0	0	0	2	4	0.29775	1
JAK3	1	1	0	1	0	0	0	3	0.29807	1
ARID5B	2	2	0	0	0	2	0	6	0.2984	1
CREBBP	0	3	0	0	0	0	0	3	0.2986	1
ZNF276	0	1	0	0	0	0	0	1	0.29952	1
SETD2	1	3	0	1	0	0	0	5	0.3006	1
FUBP1	0	0	0	0	0	0	2	2	0.30254	1
MORC2	0	1	0	0	0	0	0	1	0.30353	1
COL1A1	1	3	0	0	0	0	1	5	0.30376	1
AIP	0	1	0	0	0	0	0	1	0.30397	1
PGAP3	0	1	0	0	0	0	0	1	0.30581	1
MITF	1	4	0	0	0	0	0	5	0.30665	1
AFF3	1	2	0	0	0	0	0	3	0.30932	1
STK11	0	1	0	0	0	0	0	1	0.31005	1
SENP5	1	1	0	0	0	0	0	2	0.31257	1
RANBP17	0	2	0	1	0	0	0	3	0.31413	1
SARDH	1	2	0	0	0	0	0	3	0.31629	1
SPI1	0	1	0	0	0	0	0	1	0.31656	1
GRIN2A	2	6	0	1	0	0	0	9	0.31702	1
TNKS	0	2	0	1	0	0	0	3	0.31855	1
IKBKE	0	2	0	0	0	0	0	2	0.32182	1
FANCM	1	3	0	0	0	1	0	3	0.32313	1
NUP214	1	3	0	0	0	0	0	4	0.32475	1
GEN1	1	1	0	1	0	0	0	3	0.32572	1
SF3B1	1	2	0	0	0	0	0	3	0.32623	1
PPM1D	0	1	0	0	0	0	0	1	0.32628	1
UTP11L	0	1	0	0	0	0	0	1	0.32704	1
EED	0	1	0	0	1	0	0	2	0.32736	1
PAX8	0	1	0	0	0	0	0	1	0.32783	1
PMS1	0	0	0	1	0	0	1	2	0.32983	1
GUCY1A2	0	1	0	0	0	0	0	1	0.33104	1
NELL1	1	4	0	1	0	0	0	6	0.33173	1
KDM5A	1	2	0	0	0	0	0	3	0.33264	1
PCSK7	1	3	0	0	0	0	0	4	0.33303	1
TET3	1	2	0	0	0	0	0	3	0.33334	1
SETDB1	0	2	0	0	1	0	1	4	0.3365	1
PGR	1	1	0	1	1	0	0	4	0.3377	1
LRP6	0	2	0	0	0	0	0	2	0.3386	1
PLCG2	0	1	0	0	2	0	0	3	0.33903	1
UIMC1	0	1	0	1	0	0	0	2	0.34019	1
RHBDF2	2	3	0	0	0	0	0	5	0.34321	1
FOXL2	1	1	0	0	0	0	0	2	0.344	1
NALCN	2	4	0	1	3	0	1	11	0.34534	1
WRN	0	3	0	0	0	0	0	3	0.34603	1
CCDC18	0	2	0	0	0	0	0	2	0.34637	1
GFI1	0	1	0	0	0	0	0	1	0.3465	1
CARD11	2	3	0	0	1	0	0	6	0.34708	1
WAS	0	1	0	0	0	0	0	1	0.34743	1
GOT1	1	1	0	0	0	0	0	2	0.34764	1
SLCO1C1	1	4	0	0	0	0	1	6	0.34823	1
BLM	0	0	0	1	0	0	0	1	0.35544	1
DCC	1	2	0	0	1	0	0	4	0.35633	1
BAI3	1	6	0	0	1	0	0	8	0.35722	1
PTK2	1	2	0	0	0	0	0	3	0.3578	1
ITK	0	1	0	0	0	0	0	1	0.35866	1
NPHS2	0	1	0	0	1	0	0	2	0.36118	1
GABRA1	1	1	0	0	0	0	0	2	0.36162	1
ALDH2	1	1	0	0	0	0	0	2	0.36293	1
ERG	0	1	0	0	0	0	0	1	0.36446	1
MSN	0	1	0	0	0	0	0	1	0.36569	1
PCLO	2	8	0	2	0	1	0	13	0.36714	1

TABLE 8-continued

Gene name	n_syn	n_mis	n_non	n_lof	n_splice	n_indels_mis	n_indels_lof	num_ unique	P-value	FDR (q-value)
ITGA3	0	3	0	0	0	0	0	3	0.36749	1
ACSL3	0	1	0	0	0	0	0	1	0.36867	1
YTHDF2	0	2	0	0	0	0	0	2	0.37224	1
TUBB6	0	1	0	0	0	0	0	1	0.37345	1
BTK	0	1	0	0	0	0	0	1	0.37599	1
AHRR	0	1	0	0	0	0	0	1	0.37729	1
BDNF	0	1	0	0	0	0	0	1	0.3779	1
ZNF217	0	2	0	0	0	0	0	2	0.37868	1
GNAS	0	3	0	0	0	0	0	3	0.37877	1
REL	0	0	0	1	0	0	0	1	0.37926	1
TCF4	0	1	0	0	0	0	0	1	0.3811	1
RNASEL	0	1	0	0	0	0	0	1	0.38309	1
FOXO1	0	1	0	0	0	0	0	1	0.38541	1
CENPF	1	8	0	0	0	0	0	9	0.38686	1
PLK1	0	1	0	0	0	0	0	1	0.38752	1
TCF	0	1	0	0	0	0	0	1	0.39154	1
PIK3C2B	0	2	0	0	0	0	1	3	0.39182	1
HTR2A	0	1	0	0	0	0	0	1	0.39215	1
USP9X	0	3	0	0	0	0	1	4	0.39319	1
PRRX1	0	1	0	0	0	0	0	1	0.39486	1
AXIN2	0	0	0	0	0	0	1	1	0.39541	1
RABEP1	0	1	0	0	0	0	1	2	0.39646	1
BARD1	0	1	0	0	0	0	0	1	0.39698	1
SAMD9	0	4	0	1	0	0	0	5	0.39763	1
CDH6	0	2	0	0	1	0	0	3	0.39965	1
PFKP	1	2	0	0	0	0	0	3	0.39979	1
PAX7	0	1	0	0	0	0	0	1	0.40359	1
SMOX	0	1	0	0	0	0	0	1	0.40577	1
SCN5A	4	7	0	1	1	0	0	12	0.40615	1
CACNB2	0	0	0	1	0	1	0	2	0.40866	1
HDAC1	0	0	0	1	0	0	0	1	0.40885	1
PLCB4	0	2	0	0	1	0	0	3	0.40903	1
NOTCH2	1	2	0	1	0	1	0	5	0.41057	1
SMAD2	0	1	0	0	0	0	0	1	0.41589	1
MAP3K8	0	1	0	0	0	0	0	1	0.4207	1
CDC73	0	1	0	0	0	0	0	1	0.42116	1
FIP1L1	0	1	0	0	0	0	0	1	0.42249	1
CASC5	0	2	0	0	1	0	0	3	0.42324	1
ARNT	0	1	0	0	0	0	0	1	0.42415	1
RTEL1	0	2	0	0	0	0	0	2	0.42486	1
SLC47A1	0	1	0	0	0	0	0	1	0.42574	1
MLH1	0	3	0	1	0	0	0	4	0.4263	1
EXT2	0	1	0	0	0	0	0	1	0.42683	1
ROBO2	1	3	0	0	0	0	0	4	0.4275	1
KIF5B	1	1	0	0	0	0	0	2	0.42768	1
SLC22A2	0	1	0	0	0	0	0	1	0.42794	1
TOP2A	0	1	0	0	0	0	0	1	0.43285	1
PTK2B	1	1	0	0	1	0	0	3	0.433	1
FOXA1	0	1	0	0	0	0	0	1	0.43406	1
KLHL14	0	1	0	0	0	0	0	1	0.43414	1
ATR	0	2	0	0	0	1	0	3	0.43663	1
HNF1A	0	1	0	0	0	0	0	1	0.43666	1
PDPK1	1	1	0	0	0	0	0	2	0.43697	1
CYP2B6	1	1	0	0	0	0	0	2	0.43745	1
FANCA	0	1	0	0	0	0	0	1	0.4382	1
MET	1	1	0	0	0	0	0	2	0.43946	1
CBL	0	1	0	0	0	0	0	1	0.4398	1
BAP1	0	1	0	0	0	0	0	1	0.44006	1
CAPRIN1	0	1	0	0	0	0	0	1	0.44058	1
STAG2	0	1	0	0	0	0	0	1	0.44079	1
MAFB	0	1	0	0	0	0	0	1	0.44344	1
USP6	1	2	0	0	1	0	0	4	0.44369	1
NF2	0	1	0	0	0	0	0	1	0.4446	1
SLC15A2	0	1	0	0	0	0	0	1	0.44884	1
RNF43	0	1	0	0	0	0	0	1	0.45078	1
CRTC3	0	1	0	0	0	0	0	1	0.45188	1
SLCO2B1	1	1	0	0	0	0	0	2	0.45194	1
BCR	0	3	0	0	0	0	0	3	0.45379	1
BRCA2	2	12	0	0	0	0	0	14	0.45384	1
SLC34A2	1	1	0	0	0	0	0	2	0.45502	1
PDGFRA	1	1	0	1	1	0	0	4	0.45506	1
NFL2L2	0	1	0	0	0	0	0	1	0.45598	1
ARHGEF11	1	2	0	0	0	0	0	3	0.45732	1
SMARCA4	0	2	0	0	0	0	0	2	0.45803	1

TABLE 8-continued

Gene name	n_syn	n_mis	n_non	n_lof	n_splice	n_indels_mis	n_indels_lof	num_ unique	P-value	FDR (q-value)
AKT1	0	1	0	0	0	0	0	1	0.45826	1
SLIT2	1	2	0	0	1	0	0	4	0.4588	1
ITGB2	0	1	0	0	1	0	0	2	0.45918	1
MBD1	0	1	0	0	1	0	0	2	0.45926	1
PLCG1	2	2	0	1	0	0	0	5	0.46207	1
TAF15	0	1	0	0	0	0	0	1	0.46761	1
LRRTM4	1	1	0	0	0	0	0	2	0.46844	1
TNFAIP3	0	1	0	0	0	0	0	1	0.46867	1
DSP	0	4	0	0	0	0	0	3	0.46868	1
STIL	1	0	0	1	0	0	0	2	0.4694	1
NSD1	2	4	0	0	0	0	0	6	0.46969	1
WBSCR17	2	4	0	0	0	0	0	6	0.4722	1
ABCC2	0	3	0	1	1	0	0	5	0.47328	1
LAMP1	1	1	0	0	0	0	0	2	0.47412	1
ABCC5	1	2	0	0	0	0	0	3	0.47537	1
HECW1	3	3	0	0	0	0	0	6	0.47542	1
NCOA2	0	4	0	0	0	0	0	4	0.4758	1
DTX1	0	1	0	0	1	0	0	2	0.47635	1
PHLPP2	2	0	0	0	0	0	1	2	0.47656	1
DBH	0	1	0	0	1	0	0	2	0.47675	1
TETI	0	2	0	1	0	0	0	3	0.47755	1
PTPRS	5	4	0	0	0	1	0	10	0.4777	1
KIAA1549	2	2	0	0	0	0	0	4	0.48389	1
MRE11A	0	1	0	0	0	0	0	1	0.48749	1
SRGAP3	1	3	0	1	0	0	0	5	0.4901	1
DDR2	1	1	0	0	0	0	0	2	0.49459	1
ATP10D	2	5	0	0	0	0	1	8	0.49469	1
IL21R	0	2	0	0	0	0	0	2	0.49632	1
SLCO1B3	0	3	0	0	0	0	0	3	0.49653	1
OBSCN	7	22	0	0	1	1	1	32	0.50023	1
PCDHB6	2	1	0	0	0	0	0	3	0.50367	1
PYGL	1	1	0	0	0	0	0	2	0.50479	1
JAKMIP2	0	3	0	1	0	0	0	4	0.50785	1
RIPK1	1	1	0	1	0	0	0	3	0.50966	1
AXL	1	4	0	1	0	0	0	6	0.50979	1
BCL6	0	2	0	0	0	0	0	2	0.51026	1
SF3B2	0	1	0	0	0	0	0	1	0.51151	1
GOLGA5	0	1	0	0	0	0	0	1	0.51413	1
ZMYM2	2	1	0	0	0	0	0	3	0.52388	1
CYP1B1	1	1	0	0	0	0	0	2	0.5252	1
EPC1	0	1	0	0	0	0	0	1	0.52668	1
FOXP2	0	3	0	0	0	0	0	3	0.5292	1
NEBL	1	1	0	0	0	1	0	3	0.52942	1
ANKRD26	0	2	0	2	1	1	0	6	0.53263	1
NBN	1	3	0	0	0	0	0	4	0.53298	1
CUL1	0	1	0	0	0	0	0	1	0.53369	1
ELAC2	0	1	0	0	1	0	0	2	0.53435	1
MALT1	1	1	0	0	0	0	1	3	0.53482	1
DDX3X	0	1	0	0	0	0	0	1	0.53722	1
ERCC3	1	2	0	0	0	0	0	3	0.53957	1
CDH6	1	5	0	0	0	0	0	5	0.53984	1
NCOR1	1	2	0	1	1	0	0	5	0.54422	1
ERCC4	1	0	0	1	0	0	0	2	0.54453	1
MKI67	2	10	0	1	0	0	0	13	0.5746	1
XPC	1	1	0	0	0	0	0	2	0.54955	1
CDH2	0	3	0	0	0	0	0	3	0.55277	1
COLEC12	0	2	0	0	0	0	0	2	0.55486	1
BMPR1A	1	2	0	0	0	0	0	3	0.55526	1
FH	1	1	0	0	0	0	0	2	0.55558	1
BRD3	1	1	0	0	0	0	0	2	0.55736	1
XPO1	0	1	0	0	0	0	0	1	0.55899	1
UNC13D	0	0	0	1	0	1	0	2	0.56097	1
FGFR3	1	1	0	0	0	0	0	2	0.5615	1
ANTXR1	0	1	0	0	0	0	0	1	0.56165	1
KEAP1	1	1	0	0	0	0	0	2	0.56244	1
PIK3CG	2	3	0	0	0	0	0	5	0.56341	1
RBM15	0	2	0	0	0	0	0	2	0.56352	1
EPHB2	0	1	0	0	0	0	0	1	0.56514	1
COL1A2	2	1	0	0	1	0	0	4	0.5678	1
FGF14	1	1	0	0	0	0	0	2	0.57328	1
RNF213	2	10	0	0	1	0	0	13	0.57376	1
NRP1	0	2	0	0	0	0	0	2	0.57622	1
HAS2	0	1	0	0	0	0	0	1	0.57713	1
MLH3	0	1	0	0	0	0	0	1	0.57795	1

TABLE 8-continued

Gene name	n_syn	n_mis	n_non	n_lof	n_splice	n_indels_mis	n_indels_lof	num_ unique	P-value	FDR (q-value)
ACE	0	2	0	0	0	0	0	2	0.58057	1
BRD4	2	2	0	0	0	0	0	4	0.5876	1
RB1	0	1	0	2	0	0	0	3	0.58993	1
MYBL2	0	1	0	0	1	0	0	2	0.59065	1
DICER1	0	2	0	0	0	0	0	2	0.59491	1
ERCC2	0	1	0	0	0	0	0	1	0.59499	1
SMO	1	1	0	0	0	0	0	2	0.59778	1
BCL11A	0	1	0	0	0	0	0	1	0.60039	1
JAK2	0	2	0	0	0	0	0	2	0.60061	1
MED12	1	3	0	0	0	0	0	4	0.60339	1
CACNA1C	1	2	0	1	1	0	0	5	0.60443	1
ABCB11	0	1	0	0	0	0	0	1	0.60572	1
EPHA5	1	3	0	0	0	0	0	4	0.60734	1
THBS1	0	0	0	1	0	0	0	1	0.60782	1
PLXNA1	3	5	0	0	0	0	0	8	0.60896	1
PTPRT	2	4	0	1	0	0	0	7	0.61012	1
COL11A1	1	4	0	1	2	0	1	9	0.61069	1
NLRP1	0	0	0	1	0	0	0	1	0.61133	1
ANLN	0	0	0	1	0	0	0	1	0.61661	1
LIFR	1	3	0	0	0	0	0	4	0.61924	1
GAS7	0	1	0	0	0	0	0	1	0.61964	1
ASXLI	3	1	0	0	0	0	0	4	0.6221	1
ZSCAN20	1	2	0	0	0	0	0	3	0.62315	1
FAT2	1	6	0	0	0	0	0	7	0.62355	1
SMC1A	0	1	0	0	0	0	0	1	0.62361	1
DMD	0	6	0	3	1	0	0	10	0.62567	1
EXT1	0	3	0	1	0	0	0	4	0.62571	1
MYCN	0	1	0	0	0	0	0	1	0.63058	1
PHLDB1	0	1	0	0	0	0	0	1	0.63211	1
CES1	2	3	0	0	0	0	0	5	0.63224	1
ERC1	1	2	0	0	0	0	0	3	0.63564	1
MLLT3	1	1	0	1	0	0	0	3	0.63749	1
PIK3R2	2	1	0	0	0	0	0	3	0.63915	1
ALOX5	1	1	0	0	0	0	0	2	0.64058	1
RARA	2	2	0	0	0	0	0	4	0.64211	1
STK36	1	1	0	0	0	0	0	2	0.643	1
PLEKHG5	1	1	0	0	0	0	0	2	0.64339	1
FLT3	1	1	0	0	1	0	1	4	0.65141	1
NF1	1	6	0	0	1	1	0	9	0.65407	1
ARHGEF12	0	0	0	1	1	0	0	2	0.65428	1
TSC2	1	1	0	0	1	0	0	3	0.65455	1
FAT3	6	10	0	0	0	0	0	16	0.65699	1
DNMT1	1	2	0	0	0	0	0	3	0.65996	1
NIN	0	1	0	0	0	0	0	1	0.66257	1
PDGFRB	0	1	0	0	0	0	0	1	0.66312	1
ALK	3	4	0	0	3	0	0	9	0.66451	1
PTCH2	2	1	0	0	0	0	0	3	0.66865	1
RICTOR	0	1	0	1	1	0	0	3	0.66879	1
WHSC1	0	1	0	0	1	0	0	2	0.67667	1
SEMA5B	2	2	0	0	0	0	0	4	0.67712	1
ERBB3	0	1	0	0	0	0	0	1	0.67983	1
RIF1	2	6	0	0	0	0	0	8	0.68191	1
GLI3	3	6	0	0	0	0	0	9	0.68506	1
NPR1	1	0	0	1	0	0	0	2	0.68695	1
FLT1	2	3	0	0	0	0	0	5	0.6899	1
GOLGA4	0	2	0	0	0	0	1	3	0.69049	1
SPEN	2	3	0	1	0	0	1	7	0.69605	1
MED1	0	1	0	0	0	0	0	1	0.69607	1
HDAC4	2	1	0	0	0	0	0	3	0.69737	1
PEAR1	2	2	0	0	0	0	0	4	0.69762	1
MST1R	1	1	0	0	0	0	0	2	0.70452	1
KIT	1	4	0	0	0	0	0	5	0.70577	1
NCOA1	0	1	0	0	0	2	0	2	0.71084	1
PTCH1	0	1	0	0	1	0	0	2	0.71534	1
SMC3	0	1	0	0	1	0	0	2	0.71567	1
UBR5	1	1	0	0	0	0	0	2	0.71685	1
HIP1	1	0	0	1	1	0	0	3	0.71809	1
ERCC5	1	2	0	1	0	0	0	4	0.71841	1
ZBTB16	2	2	0	0	1	0	1	6	0.71983	1
NCOR2	1	3	0	0	0	0	0	4	0.72473	1
NR3C1	0	1	0	0	0	0	0	1	0.72588	1
INSR	1	2	0	0	0	0	0	3	0.7281	1
NDRG1	1	1	0	0	0	0	0	2	0.72947	1
MYO18A	3	1	0	0	1	0	0	5	0.73563	1

TABLE 8-continued

Gene name	n_syn	n_mis	n_non	n_lof	n_splice	n_indels_mis	n_indels_lof	num_ unique	P-value	FDR (q-value)
PKHD1	3	10	0	0	0	0	0	13	0.7378	1
STAT5A	0	1	0	0	0	0	0	1	0.74112	1
PDE4DIP	4	9	0	2	1	0	0	16	0.7431	1
PIK3CD	1	1	0	0	1	0	0	3	0.74804	1
MAP3K1	2	2	0	1	2	0	0	7	0.75112	1
KIF1B	0	2	0	0	0	0	0	2	0.75594	1
ADAMTS20	3	4	0	0	0	0	0	7	0.75809	1
XIRP2	7	15	0	0	0	0	0	22	0.7609	1
LRRFIP1	1	1	0	0	0	0	0	2	0.76522	1
PTGS2	1	2	0	0	0	0	0	3	0.76652	1
MYH9	4	2	0	0	0	0	0	6	0.76717	1
ZNF521	1	1	0	0	0	0	0	2	0.76959	1
RIPK4	2	1	0	0	0	0	0	3	0.77303	1
WRAP53	2	1	0	0	0	0	0	3	0.77524	1
GRM8	0	2	0	0	0	0	0	2	0.77532	1
TERT	2	1	0	0	0	0	0	3	0.77924	1
DOT1L	0	2	0	0	0	0	0	2	0.78239	1
FAT4	5	9	0	0	0	0	0	14	0.78626	1
RET	1	2	0	0	0	0	0	3	0.78774	1
APOB	4	5	0	2	0	0	1	12	0.79118	1
SRRM2	2	4	0	1	0	0	1	8	0.79925	1
MTR	1	2	0	0	0	0	0	3	0.80002	1
FAT1	4	8	0	1	0	0	0	13	0.80428	1
ITPKB	2	1	0	0	0	0	0	3	0.80509	1
RAD21	2	2	0	0	0	0	0	4	0.80568	1
NOTCH3	1	2	0	0	0	0	0	3	0.80664	1
MECOM	2	0	0	0	0	0	1	3	0.80729	1
TET2	1	1	0	0	0	0	0	2	0.81506	1
BRCA1	1	1	0	2	0	0	0	4	0.82338	1
AKAP12	1	2	0	1	0	0	0	4	0.83113	1
NTRK1	2	2	0	0	0	0	0	4	0.83151	1
ATRX	1	3	0	0	0	0	0	4	0.83899	1
ITGA9	3	2	0	0	0	0	0	5	0.84206	1
EPHA7	2	4	0	1	0	0	0	7	0.84363	1
MYOM2	0	1	0	0	0	0	0	1	0.84404	1
EVPL	0	1	0	0	0	0	1	2	0.84507	1
RPTOR	2	1	0	0	0	0	0	3	0.84992	1
POLE	2	4	0	0	0	0	0	6	0.85235	1
DPYD	2	4	0	0	0	0	0	6	0.8554	1
PTGS1	0	1	0	1	0	0	0	2	0.85895	1
PTPRD	2	2	0	0	0	0	0	4	0.86366	1
TAF1	0	1	0	0	2	0	0	3	0.87126	1
FN1	4	4	0	0	1	2	0	11	0.87225	1
CBLB	2	3	0	2	0	0	0	7	0.87889	1
MAGI1	0	3	0	0	0	0	0	3	0.8893	1
CTNNA1	2	1	0	0	1	0	0	4	0.89081	1
EPHA3	1	1	0	0	1	0	0	3	0.89152	1
CLCA2	3	2	0	0	0	0	0	5	0.89364	1
LRP5	2	1	0	0	1	0	0	4	0.90452	1
SUFU	1	1	0	0	0	0	0	2	0.90698	1
CACNA2D1	2	2	0	0	0	1	0	5	0.91361	1
ERBB4	0	0	0	1	0	0	0	1	0.91636	1
FLT4	4	3	0	0	0	0	0	7	0.91808	1
ROS1	2	3	0	0	1	0	0	6	0.91814	1
USP42	1	2	0	0	0	0	0	3	0.92166	1
MUC16	12	31	0	2	0	1	0	46	0.92619	1
ARHGEF7	2	2	0	0	0	0	0	4	0.92895	1
ARID1A	1	2	0	2	0	0	1	6	0.9312	1
MLLT4	2	0	0	0	1	0	0	3	0.9318	1
PRF1	2	3	0	0	0	0	0	5	0.93429	1
SYNE1	11	27	0	3	0	3	0	43	0.03909	1
MTOR	2	2	0	0	0	0	0	4	0.034469	1
TRIM24	0	1	0	1	0	0	0	2	0.034714	1
HOXC13	1	1	0	0	0	0	0	2	0.035026	1
PCDH9	3	10	0	2	0	0	0	15	0.035126	1
MXRA5	5	4	0	0	0	0	0	9	0.035246	1
ATP10A	3	4	0	0	1	0	0	8	0.035282	1
ZNF423	2	3	0	0	0	0	0	5	0.036271	1
IGF2R	1	0	0	1	0	0	0	2	0.036893	1
FASN	0	3	0	0	1	0	0	4	0.037462	1
PTPRC	4	3	0	0	0	0	1	8	0.09762	1
DAB2IP	2	2	0	0	0	0	0	4	0.97809	1
MYH11	3	1	0	0	0	0	0	4	0.98944	1
MAP2K2	2	1	0	0	0	0	0	3	0.99099	1

TABLE 8-continued

Gene name	n_syn	n_mis	n_non	n_lof	n_splice	n_indels_mis	n_indels_lof	num_ unique	P-value	FDR (q-value)
CYP3A4	1	1	0	0	0	0	0	2	0.9935	1
ATM	0	8	0	2	1	0	0	11	0.99384	1
SDHA	3	3	0	0	0	0	0	6	0.99544	1
AR	4	5	0	0	0	0	0	9	0.99653	1
GPR98	2	13	0	0	2	1	1	19	0.99704	1
TAL2	1	1	0	0	0	0	0	2	0.99913	1
POR	1	1	0	0	0	0	0	2	0.99932	1
PRDM16	2	1	0	0	0	0	0	3	0.99978	1
EP400	7	6	0	1	0	0	0	12	0.99997	1
SIGLEC10	3	1	0	0	0	0	0	4	0.99999	1
NUMA1	0	5	0	0	0	0	0	5	0.99999	1
MKL1	4	2	0	0	0	0	0	6	1	1
TRRAP	4	7	0	0	1	0	0	10	1	1
ARID3B	4	1	0	0	0	0	0	5	1	1
ABCG2	1	0	0	0	0	0	0	1	1	1
ABL1	3	0	0	0	0	0	0	3	1	1
ACVR1B	1	0	0	0	0	1	0	2	1	1
ADAMTSL3	3	0	0	0	0	0	0	3	1	1
ADD3	1	0	0	0	0	0	0	1	1	1
AFF4	0	0	0	0	1	0	0	1	1	1
AHR	1	0	0	0	0	0	0	1	1	1
AIM2	0	0	0	0	2	0	0	2	1	1
ARHGAP26	0	0	0	0	0	0	1	1	1	1
ARID4B	2	0	0	0	0	0	0	2	1	1
AURKB	1	0	0	0	0	0	0	1	1	1
BCL2A1	1	0	0	0	0	0	0	1	1	1
BCOR	1	0	0	0	0	0	0	1	1	1
BNIP3	0	0	0	0	1	0	0	1	1	1
CCND3	0	0	0	0	1	0	0	1	1	1
CD274	1	0	0	0	0	0	0	1	1	1
CD36	1	0	0	0	0	0	0	1	1	1
CD44	1	0	0	0	0	0	0	1	1	1
CD8A	2	0	0	0	0	0	0	2	1	1
CDKN2A	0	0	0	1	0	0	0	1	1	1
CDKN3	1	0	0	0	0	0	0	1	1	1
CDX2	0	0	0	0	0	1	0	1	1	1
CHCHD7	0	1	0	0	0	0	0	1	1	1
CHD1	1	0	0	0	1	0	0	2	1	1
CTNNA3	4	0	0	0	0	0	0	4	1	1
CUX1	2	0	0	0	0	0	0	2	1	1
DDX41	0	0	0	0	0	0	1	1	1	1
DDX5	1	0	0	0	0	0	0	1	1	1
DDX6	1	0	0	0	0	0	0	1	1	1
DRD2	2	0	0	0	0	0	0	2	1	1
EIF4A2	0	0	0	0	1	0	0	1	1	1
ELK4	0	1	0	0	0	0	0	1	1	1
ELN	0	0	0	0	0	1	0	1	1	1
EPHA10	1	0	0	0	0	0	0	1	1	1
EPHA2	1	0	0	0	0	0	0	1	1	1
ETS1	1	0	0	0	0	0	0	1	1	1
FADD	1	0	0	0	0	0	0	1	1	1
FANCB	0	0	0	0	1	0	0	1	1	1
FANCD2	0	0	0	0	1	0	3	2	1	1
FANCE	2	0	0	0	0	0	0	2	1	1
FANCF	1	0	0	0	0	0	0	1	1	1
FANCI	1	0	0	0	0	0	0	1	1	1
FBXO11	1	0	0	0	1	0	0	2	1	1
FGFR1	1	0	0	0	0	0	0	1	1	1
FGFR2	2	0	0	0	0	0	0	2	1	1
FGFR4	1	0	0	0	0	0	0	1	1	1
FUS	1	0	0	0	0	0	0	1	1	1
FZR1	0	0	0	0	1	0	0	1	1	1
GBGT1	0	0	0	0	0	1	0	1	1	1
GIT2	0	0	0	0	1	0	0	1	1	1
GLMN	1	0	0	0	0	4	0	2	1	1
GMPS	1	0	0	0	1	0	0	2	1	1
GNA11	1	0	0	0	0	0	0	1	1	1
GRK4	2	0	0	0	0	0	0	2	1	1
GSK3B	0	0	0	0	0	0	1	1	1	1
HAX1	1	0	0	0	0	0	0	1	1	1
HEXIM1	1	0	0	0	0	0	0	1	1	1
HIST1H4I	1	0	0	0	0	0	0	1	1	1
HRAS	1	0	0	0	0	0	0	1	1	1
IKZF1	3	0	0	0	0	0	0	3	1	1

TABLE 8-continued

Gene name	n_syn	n_mis	n_non	n_lof	n_splice	n_indels_mis	n_indels_lof	num_ unique	P-value	FDR (q-value)
JUN	1	0	0	0	0	0	0	1	1	1
KCNH2	1	0	0	0	0	0	0	1	1	1
KDM5C	1	0	0	0	1	0	0	2	1	1
KDM6A	0	0	0	0	0	0	2	1	1	1
KL	0	0	0	0	0	0	1	1	1	1
KLF4	1	0	0	0	0	0	0	1	1	1
LHFP	2	0	0	0	1	0	0	3	1	1
LMO1	1	0	0	0	0	0	0	1	1	1
LTBP2	1	0	0	0	0	0	0	1	1	1
LTK	1	0	0	0	0	0	1	2	1	1
MARK4	0	0	0	0	1	0	0	1	1	1
MC1R	2	0	0	0	0	0	0	2	1	1
MDM4	2	1	0	0	0	0	0	3	1	1
MEF2D	1	0	0	0	0	0	0	1	1	1
MEN1	1	0	0	0	0	0	0	1	1	1
MLLT1	1	0	0	0	0	0	0	1	1	1
MLLT10	1	0	0	0	0	0	0	1	1	1
MLLT6	1	0	0	0	0	0	0	1	1	1
MMP2	1	0	0	0	0	0	0	1	1	1
MRPL3	1	0	0	0	0	0	0	1	1	1
MSR1	1	0	0	0	1	0	0	2	1	1
NFIB	0	2	0	0	0	0	0	2	1	1
NFKB2	1	0	0	0	0	0	0	1	1	1
NOTCH1	3	2	0	1	0	0	0	6	1	1
P4HA2	1	0	0	0	0	0	0	1	1	1
PARP1	1	0	0	0	0	0	0	1	1	1
PAX5	0	0	0	0	2	0	0	2	1	1
PBRM1	1	0	0	0	0	0	0	1	1	1
PEG3	1	0	0	0	0	0	0	1	1	1
PER1	1	0	0	0	0	1	0	2	1	1
PHOX2B	1	0	0	0	0	0	0	1	1	1
PIM1	1	1	0	0	0	0	0	1	1	1
PML	2	0	0	0	0	0	0	2	1	1
PMS2	1	0	0	0	0	0	0	1	1	1
PTPRJ	2	0	0	0	0	0	0	2	1	1
PXN	0	1	0	0	0	0	0	1	1	1
RAD51	1	0	0	0	0	0	0	1	1	1
RGS20	2	0	0	0	0	0	0	2	1	1
RRM1	0	0	0	0	1	0	0	1	1	1
SBF2	1	0	0	0	0	0	1	2	1	1
SFXN4	0	0	0	0	1	0	0	1	1	1
SLC16A1	0	2	0	0	0	0	0	1	1	1
SLC22A3	1	0	0	0	0	0	0	1	1	1
SLC38A3	0	1	0	0	0	0	0	1	1	1
SLC6A3	0	0	0	0	1	0	0	1	1	1
SLC9A3R1	0	0	0	0	1	0	0	1	1	1
SMAD6	1	0	0	0	0	0	0	1	1	1
SNX2	1	0	0	0	0	0	0	1	1	1
SNX29	2	0	0	0	0	0	0	1	1	1
SOCS3	1	0	0	0	0	0	0	1	1	1
STAT1	2	0	0	0	0	0	0	2	1	1
STAT5B	2	0	0	0	0	0	0	2	1	1
STXBP2	0	0	0	0	1	0	0	1	1	1
SYK	1	0	0	0	0	0	0	1	1	1
T	0	1	0	0	0	0	0	1	1	1
TBX22	0	0	0	0	1	0	0	1	1	1
TCF12	2	0	0	0	0	0	0	1	1	1
TCL1A	1	0	0	0	0	0	0	1	1	1
TFRC	1	0	0	0	0	0	0	1	1	1
TNFRSF13B	1	0	0	0	0	0	0	1	1	1
TNKS2	3	0	0	0	0	0	0	3	1	1
TPM3	1	0	0	0	0	0	0	1	1	1
TRAF7	2	1	0	0	0	0	0	3	1	1
TRIP11	0	0	0	0	1	0	0	1	1	1
TSHR	0	0	0	0	1	0	0	1	1	1
TYK2	2	0	0	0	0	0	0	2	1	1
VKORC1	1	0	0	0	0	0	0	1	1	1
ZMIZ1	2	0	0	0	0	0	0	2	1	1
SEPT2	0	1	0	0	0	0	0	1	1	1
SEPT6	0	1	0	1	0	0	0	2	1	1
SEPT9	0	1	0	0	1	0	0	2	1	1
ACKR3	2	0	0	0	0	0	0	2	1	1
AMER1	0	3	0	2	0	0	0	5	1	1
ARHGEF26	1	2	0	0	0	0	0	3	1	1

TABLE 8-continued

Gene name	n_syn	n_mis	n_non	n_lof	n_splice	n_indels_mis	n_indels_lof	num_ unique	P-value	FDR (q-value)
BIVM-ERCC5	1	2	0	1	0	0	0	4	1	1
C12orf79	0	0	0	0	1	0	0	1	1	1
CNTRL	0	1	0	0	0	0	0	1	1	1
DEPTOR	0	1	0	0	0	0	0	1	1	1
DROSHA	2	2	0	0	0	2	1	6	1	1
ENKD1	0	1	0	0	0	0	0	1	1	1
KAT6A	0	2	0	0	0	0	0	2	1	1
KAT6B	1	1	0	0	0	0	0	2	1	1
KHDC3L	0	0	0	0	1	0	0	1	1	1
KMT2A	1	3	0	0	0	0	0	4	1	1
KMT2B	1	4	0	0	0	0	0	5	1	1
KMT2C	0	7	0	0	0	0	1	9	1	1
KMT2D	2	4	0	1	0	0	0	6	1	1
LOC100129083	0	0	0	1	0	0	0	1	1	1
LRIF1	0	2	0	0	0	0	1	3	1	1
MEF2BNB-MEF2B	0	1	0	0	0	0	0	1	1	1
MRGBP	1	0	0	0	0	0	0	1	1	1
NOA1	0	1	0	0	0	0	0	1	1	1
NUTM1	0	1	0	0	0	0	0	1	1	1
RPS10-NUDT3	0	1	0	1	0	0	0	2	1	1
SLCO1B7	0	2	0	0	0	0	0	2	1	1
SLX4	1	2	0	0	0	0	0	3	1	1
SPECC1	0	3	0	0	0	0	0	3	1	1
SRSF2	0	1	0	0	0	0	0	1	1	1
SRSF3	0	1	0	0	0	0	0	1	1	1

[0128] Table 9: Genomic alterations unique to each SNF subtype. Differentially enriched mutations and gene-level copy number variations are presented. Analysis of gene-level copy number variations was performed for those genes identified by TCGA in primary colorectal cancers[25]. Overall, analyses were performed for genomic aberrations with at least 20% frequency in at least one SNF subtype. Statistical significance was determined using Fisher's exact tests between each SNF group versus the remaining two SNF groups.

TABLE 9

Genomic Aberration	SNF1	SNF2	SNF3	Comparison	P-value
NOTCH1 mutation	23.1%	0.0%	0.0%	SNF1v2,3	0.0232
PIK3C2B mutation	23.1%	0.0%	0.0%	SNF1v2,3	0.0232
CDK12 mutation	0.0%	20.0%	0.0%	SNF2v1,3	0.0369
EBF1 mutation	0.0%	20.0%	0.0%	SNF2v1,3	0.0369
NRAS mutation	0.0%	20.0%	0.0%	SNF2v1,3	0.0369
DMD mutation	0.0%	26.7%	6.7%	SNF2v1,3	0.0428
VEGFA amplification	46.2%	6.7%	40.0%	SNF2v1,3	0.017
SMAD3 mutation	0.0%	0.0%	20.0%	SNF3v1,2	0.0369

[0129] Tables 10A-C: Table 10A lists genes whose expression is analyzed in a classification model for identifying SNF2 metastases. The difference in gene expression ("Log 2FC" column) between SNF2 metastases as compared to SNF1 and SNF3 metastases is shown, along with the function or pathway associated with each gene. Table 10B lists the genes in Table 10A that are expressed at a significantly higher level in SNF2 metastases than in SNF1 and SNF3 metastases. Table 10C lists the genes in Table 10A that are expressed at a significantly lower level in SNF2 metastases than in SNF1 and SNF3 metastases.

TABLE 10A

ENSEMBL ID	Gene Symbol	log2FC (SNF2 vs. SNF1, 3)	Function/Pathway
ENSG00000082438	COBLL1	−0.800881317	Actin binding
ENSG00000170417	TMEM182	−1.045618291	Adipogenesis; myogenesis
ENSG00000176720	BOK	1.690960733	Apoptosis; Development
ENSG00000156171	DRAM2	−0.851968947	Autophagy
ENSG00000140941	MAP1LC3B	−0.735698571	Autophagy
ENSG00000129467	ADCY4	1.220343115	cAMP formation
ENSG00000076662	ICAM3	1.368014118	Cell adhesion
ENSG00000164162	ANAPC10	−0.746014397	Cell cycle
ENSG00000107443	CCNJ	−0.890337582	Cell cycle
ENSG00000132466	ANKRD17	−0.533617194	Cell differentiation
ENSG00000129474	AJUBA	1.046456583	Cell proliferation and differentiation
ENSG00000105518	TMEM205	0.879144662	Cisplatin resistance
ENSG00000134318	ROCK2	−1.026390625	Cytokinesis; focal adhesions; cytoskeleton

TABLE 10A-continued

ENSEMBL ID	Gene Symbol	log2FC (SNF2 vs. SNF1, 3)	Function/Pathway
ENSG00000116127	ALMS1	−0.723286687	Cytoskeleton
ENSG00000120860	CCDC53	−0.761708434	Cytoskeleton; Endosome
ENSG00000089094	KDM2B	0.758836161	Demethylation
ENSG00000144468	RHBDD1	−0.537760383	Endopeptidase
ENSG00000179044	EXOC3L1	1.566820255	Exocytosis
ENSG00000181031	RPH3AL	0.988775688	Exocytosis
ENSG00000080573	COL5A3	1.413644796	Extracellular matrix formation
ENSG00000205864	KRTAP5-6	1.987671868	Extracellular matrix formation
ENSG00000183153	GJD3	2.478515517	Gap junctions
ENSG00000138604	GLCE	−1.04250676	Glycosaminoglycan metabolism
ENSG00000115806	GORASP2	−0.428318392	Golgi function
ENSG00000165801	ARHGEF40	0.997555327	G-protein receptor signaling
ENSG00000065135	GNAI3	−0.757257708	G-protein receptor signaling
ENSG00000172380	GNG12	−0.836333361	G-protein receptor signaling
ENSG00000132518	GUCY2D	2.393664098	G-protein receptor signaling
ENSG00000189410	SH2D5	2.394773121	G-protein receptor signaling
ENSG00000170647	TMEM133	−1.262797743	G-protein receptor signaling
ENSG00000158062	UBXN11	0.948861211	G-protein receptor signaling
ENSG00000162694	EXTL2	−0.92833322	Heparin modification
ENSG00000181045	SLC26A11	1.048138867	Homeostasis; electrolyte balance
ENSG00000177663	IL17RA	0.571310231	Immune response
ENSG00000155099	TMEM55A	−0.841200023	Inositol phosphate metabolism
ENSG00000125629	INSIG2	−0.868043988	Lipid metabolism
ENSG00000144182	LIPT1	−1.120043984	Lipid metabolism
ENSG00000110921	MVK	1.023529085	Lipid metabolism
ENSG00000182378	PLCXD1	1.44049891	Lipid metabolism
ENSG00000167705	RILP	1.346192582	Lysosome function
ENSG00000162600	OMA1	−0.979926283	Metalloprotease
ENSG00000168906	MAT2A	−0.571058603	Methionine adenosyltransferase activity
ENSG00000198130	HIBCH	−0.782578708	Mitochondrial function; viral infection
ENSG00000148339	SLC25A25	1.081771899	Mitochondrial transport
ENSG00000068796	KIF2A	−0.865443147	Mitosis
ENSG00000175470	PPP2R2D	0.704123126	Mitosis
ENSG00000100968	NFATC4	1.330059279	Motility
ENSG00000118965	WDR35	−1.127339428	Motility; Sonic Hedgehog signaling
ENSG00000186654	PRR5	0.869634036	mTOR signaling
ENSG00000173786	CNP	0.776165238	Nucleic acid binding
ENSG00000121058	COIL	−0.705992325	Organelle formation
ENSG00000204160	ZDHHC18	0.82799159	Palmitoyltransferase
ENSG00000090975	PITPNM2	1.075064848	Phosphatidylinositol transfer
ENSG00000227345	PARG	−0.512288313	Poly (ADP-ribose) catabolism
ENSG00000141161	UNC45B	2.270982748	Protein chaperone
ENSG00000240344	PPIL3	−0.86000924	Protein folding
ENSG00000178904	DPY19L3	−0.805965771	Protein modification
ENSG00000121350	PYROXD1	−0.982117531	Protein modification
ENSG00000155304	HSPA13	−0.97308995	Protein processing
ENSG00000107902	LHPP	1.035307778	Purine metabolism
ENSG00000222014	RAB6C|WTH3DI	−2.099593453	RAS signaling
ENSG00000010017	RANBP9	−0.714562753	RAS signaling
ENSG00000023572	GLRX2	−0.859346451	Redox signaling
ENSG00000130244	FAM98C	0.893820425	RNA binding
ENSG00000180917	CMTR2	−0.875904403	RNA modification
ENSG00000185716	C16orf521|LOC102725138	−0.949150607	Sonic hedgehog signaling
ENSG00000203965	EFCAB7	−1.089559098	Sonic hedgehog signaling
ENSG00000124380	SNRNP27	−0.627397765	Splicing
ENSG00000112305	SMAP1	−0.624975625	Stromal cell activation
ENSG00000164506	STXBP5	−0.974501473	Synaptic vesicles
ENSG00000121989	ACVR2A	−1.051537003	TGF-beta signaling
ENSG00000223802	GDF1|CERS1	1.844243212	TGF-beta signaling
ENSG00000157933	SKI	0.696032727	TGF-beta signaling
ENSG00000136603	SKIL	−1.090266877	TGF-beta signaling
ENSG00000179348	GATA2	1.867742578	Transcription; immune signaling
ENSG00000160741	CRTC2	0.605701789	Transcriptional regulation
ENSG00000141979	CTD-3222D19.2 (Clone-based (Vega) gene)	−2.076024446	Transcriptional regulation
ENSG00000198746	GPATCH3	0.827826305	Transcriptional regulation
ENSG00000119669	IRF2BPL	1.115703855	Transcriptional regulation
ENSG00000140044	JDP2	1.005345222	Transcriptional regulation
ENSG00000116044	NFE2L2	−0.592450472	Transcriptional regulation
ENSG00000080298	RFX3	−0.869749954	Transcriptional regulation

TABLE 10A-continued

ENSEMBL ID	Gene Symbol	log2FC (SNF2 vs. SNF1, 3)	Function/Pathway
ENSG00000085721	RRN3	−0.702609197	Transcriptional regulation
ENSG00000111832	RWDD1	−0.796074992	Transcriptional regulation
ENSG00000087266	SH3BP2	0.755613904	Transcriptional regulation
ENSG00000115750	TAF1B	−0.804267724	Transcriptional regulation
ENSG00000184517	ZFP1	−0.709320083	Transcriptional regulation
ENSG00000213096	ZNF254	−1.210045897	Transcriptional regulation
ENSG00000181315	ZNF322	−0.803566951	Transcriptional regulation
ENSG00000083838	ZNF446	0.9935166	Transcriptional regulation
ENSG00000132677	RHBG	2.904694676	Transmembrane protein transport
ENSG00000075790	BCAP29	−1.010689151	Transport
ENSG00000138036	DYNC2LI1	−0.889841056	Transport
ENSG00000068697	LAPTM4A	−0.632250511	Transport
ENSG00000174327	SLC16A13	1.083425693	Transport
ENSG00000196950	SLC39A10	−0.96271217	Transport
ENSG00000167703	SLC43A2	1.086260232	Transport
ENSG00000167645	YIF1B	1.033798947	Transport
ENSG00000130222	GADD45G	2.063438246	Tumor suppressor; cell cycle; apoptosis; senescence
ENSG00000145569	FAM105A	−1.454434258	Ubiquitin modification
ENSG00000151116	UEVLD	−0.758631616	Ubiquitin modification
ENSG00000182670	TTC3	−0.815325423	Ubiquitin modification; Akt signaling
ENSG00000175104	TRAF6	−0.672175695	Ubiquitin modification; immune response
ENSG00000077232	DNAJC10	−0.75940466	Unfolded protein binding
ENSG00000110011	DNAJC4	0.839114239	Unfolded protein binding
ENSG00000137720	C11orf1	−1.041150318	Unknown
ENSG00000159761	C16orf86	1.728334231	Unknown
ENSG00000108021	FAM208B	−0.607079753	Unknown
ENSG00000059122	FLYWCH1	1.023031667	Unknown
ENSG00000113638	TTC33	−1.011428566	Unknown
ENSG00000146574	CCZ1B	−1.044675474	Vesicle transport
ENSG00000280433	LOC102724200	−1.459202933	Vesicle transport
ENSG00000111906	HDDC2	−0.933634846	Viral infection

TABLE 10B

ENSEMBL ID	Gene Symbol	log2FC (SNF2 vs. SNF1, 3)
ENSG00000176720	BOK	1.690960733
ENSG00000129467	ADCY4	1.220343115
ENSG00000076662	ICAM3	1.368014118
ENSG00000129474	AJUBA	1.046456583
ENSG00000105518	TMEM205	0.879144662
ENSG00000089094	KDM2B	0.758836161
ENSG00000179044	EXOC3L1	1.566820255
ENSG00000181031	RPH3AL	0.988775688
ENSG00000080573	COL5A3	1.413644796
ENSG00000205864	KRTAP5-6	1.987671868
ENSG00000183153	GJD3	2.478515517
ENSG00000165801	ARHGEF40	0.997555327
ENSG00000132518	GUCY2D	2.393664098
ENSG00000189410	SH2D5	2.394773121
ENSG00000158062	UBXN11	0.948861211
ENSG00000181045	SLC26A11	1.048138867
ENSG00000177663	IL17RA	0.571310231
ENSG00000110921	MVK	1.023529085
ENSG00000182378	PLCXD1	1.44049891
ENSG00000167705	RILP	1.346192582
ENSG00000148339	SLC25A25	1.081771899
ENSG00000175470	PPP2R2D	0.704123126
ENSG00000100968	NFATC4	1.330059279
ENSG00000186654	PRR5	0.869634036
ENSG00000173786	CNP	0.776165238
ENSG00000204160	ZDHHC18	0.82799159
ENSG00000090975	PITPNM2	1.075064848
ENSG00000141161	UNC45B	2.270982748
ENSG00000107902	LHPP	1.035307778
ENSG00000130244	FAM98C	0.893820425
ENSG00000223802	GDF1|CERS1	1.844243212
ENSG00000157933	SKI	0.696032727
ENSG00000179348	GATA2	1.867742578
ENSG00000160741	CRTC2	0.605701789
ENSG00000198746	GPATCH3	0.827826305
ENSG00000119669	IRF2BPL	1.115703855
ENSG00000140044	JDP2	1.005345222
ENSG00000087266	SH3BP2	0.755613904
ENSG00000083838	ZNF446	0.9935166
ENSG00000132677	RHBG	2.904694676
ENSG00000174327	SLC16A13	1.083425693
ENSG00000167703	SLC43A2	1.086260232
ENSG00000167645	YIF1B	1.033798947
ENSG00000130222	GADD45G	2.063438246
ENSG00000110011	DNAJC4	0.839114239
ENSG00000159761	C16orf86	1.728334231
ENSG00000059122	FLYWCH1	1.023031667

TABLE 10C

ENSEMBL ID	Gene Symbol	log2FC (SNF2 vs. SNF1, 3)
ENSG00000082438	COBLL1	−0.800881317
ENSG00000170417	TMEM182	−1.045618291
ENSG00000156171	DRAM2	−0.851968947
ENSG00000140941	MAP1LC3B	−0.735698571
ENSG00000164162	ANAPC10	−0.746014397
ENSG00000107443	CCNJ	−0.890337582
ENSG00000132466	ANKRD17	−0.533617194

TABLE 10C-continued

ENSEMBL ID	Gene Symbol	log2FC (SNF2 vs. SNF1, 3)
ENSG00000134318	ROCK2	−1.026390625
ENSG00000116127	ALMS1	−0.723286687
ENSG00000120860	CCDC53	−0.761708434
ENSG00000144468	RHBDD1	−0.537760383
ENSG00000138604	GLCE	−1.04250676
ENSG00000115806	GORASP2	−0.428318392
ENSG00000065135	GNAI3	−0.757257708
ENSG00000172380	GNG12	−0.836333361
ENSG00000170647	TMEM133	−1.262797743
ENSG00000162694	EXTL2	−0.92833322
ENSG00000155099	TMEM55A	−0.841200023
ENSG00000125629	INSIG2	−0.868043988
ENSG00000144182	LIPT1	−1.120043984
ENSG00000162600	OMA1	−0.979926283
ENSG00000168906	MAT2A	−0.571058603
ENSG00000198130	HIBCH	−0.782578708
ENSG00000068796	KIF2A	−0.865443147
ENSG00000118965	WDR35	−1.127339428
ENSG00000121058	COIL	−0.705992325
ENSG00000227345	PARG	−0.512288313
ENSG00000240344	PPIL3	−0.86000924
ENSG00000178904	DPY19L3	−0.805965771
ENSG00000121350	PYROXD1	−0.982117531
ENSG00000155304	HSPA13	−0.97308995
ENSG00000222014	RAB6C|WTH3DI	−2.099593453
ENSG00000010017	RANBP9	−0.714562753
ENSG00000023572	GLRX2	−0.859346451
ENSG00000180917	CMTR2	−0.875904403
ENSG00000185716	C16orf52|LOC102725138	−0.949150607
ENSG00000203965	EFCAB7	−1.089559098
ENSG00000124380	SNRNP27	−0.627397765
ENSG00000112305	SMAP1	−0.624975625
ENSG00000164506	STXBP5	−0.974501473
ENSG00000121989	ACVR2A	−1.051537003
ENSG00000136603	SKIL	−1.090266877
ENSG00000141979	CTD-3222D19.2 (Clone-based (Vega) gene)	−2.076024446
ENSG00000116044	NFE2L2	−0.592450472
ENSG00000080298	RFX3	−0.869749954
ENSG00000085721	RRN3	−0.702609197
ENSG00000111832	RWDD1	−0.796074992
ENSG00000115750	TAF1B	−0.804267724
ENSG00000184517	ZFP1	−0.709320083
ENSG00000213096	ZNF254	−1.210045897
ENSG00000181315	ZNF322	−0.803566951
ENSG00000075790	BCAP29	−1.010689151
ENSG00000138036	DYNC2LI1	−0.889841056
ENSG00000068697	LAPTM4A	−0.632250511
ENSG00000196950	SLC39A10	−0.96271217
ENSG00000145569	FAM105A	−1.454434258
ENSG00000151116	UEVLD	−0.758631616
ENSG00000182670	TTC3	−0.815325423
ENSG00000175104	TRAF6	−0.672175695
ENSG00000077232	DNAJC10	−0.75940466
ENSG00000137720	C11orf1	−1.041150318
ENSG00000108021	FAM208B	−0.607079753
ENSG00000113638	TTC33	−1.011428566
ENSG00000146574	CCZ1B	−1.044675474
ENSG00000280433	LOC102724200	−1.459202933
ENSG00000111906	HDDC2	−0.933634846

[0130] Tables 11A-C: Table 11A lists miRNAs whose expression is analyzed in a classification model for identifying SNF2 metastases. The difference in miRNA expression ("Log 2FC" column) between SNF2 metastases as compared to SNF1 and SNF3 metastases is shown. Table 11B lists the miRNAs in Table 11A that are expressed at a significantly higher level in SNF2 metastases than in SNF1 and SNF3 metastases. Table 11C lists the miRNAs in Table 11A that are expressed at a significantly lower levels in SNF2 metastases than in SNF1 and SNF3 metastases.

TABLE 11A

Probe Set Name	Transcript ID	log2FC (SNF2 vs. SNF1, 3)
MIMAT0000418_st	hsa-miR-23b-3p	−0.973911144
MIMAT0000103_st	hsa-miR-106a-5p	−0.940091903
MIMAT0000065_st	hsa-let-7d-5p	−0.855624818
MIMAT0001080_st	hsa-miR-196b-5p	−0.766240429
MIMAT0000264_st	hsa-miR-203a	−0.763078462
MIMAT0000086_st	hsa-miR-29a-3p	−0.735033964
MIMAT0000222_st	hsa-miR-192-5p	−0.714440376
MIMAT0022259_st	hsa-miR-5100	−0.69282742
MIMAT0000066_st	hsa-let-7e-5p	−0.672530325
MIMAT0000259_st	hsa-miR-182-5p	−0.648299131
MIMAT0000093_st	hsa-miR-93-5p	−0.644062486
MIMAT0000318_st	hsa-miR-200b-3p	−0.641440676
MIMAT0000076_st	hsa-miR-21-5p	−0.636319688
MIMAT0000101_st	hsa-miR-103a-3p	−0.635289418
MIMAT0000080_st	hsa-miR-24-3p	−0.599049459
MIMAT0000691_st	hsa-miR-130b-3p	−0.549958054
MIMAT0000278_st	hsa-miR-221-3p	−0.527703234
MIMAT0000243_st	hsa-miR-148a-3p	−0.445186581
MIMAT0000415_st	hsa-let-7i-5p	−0.407014793
MIMAT0000071_st	hsa-miR-17-3p	−0.307974314
MIMAT0001620_st	hsa-miR-200a-5p	−0.260909679
MIMAT0018967_st	hsa-miR-4448	−0.253668944
MIMAT0018179_st	hsa-miR-3907	0.172170872
MIMAT0027492_st	hsa-miR-6796-5p	0.180916714
MIMAT0027423_st	hsa-miR-6761-3p	0.181240609
MIMAT0022979_st	hsa-miR-4750-3p	0.191503329
MIMAT0007882_st	hsa-miR-1909-5p	0.223357116
MIMAT0026741_st	hsa-miR-1251-3p	0.258013283
MIMAT0000242_st	hsa-miR-129-5p	0.27251568
MIMAT0015070_st	hsa-miR-3188	0.27589605
MIMAT0019809_st	hsa-miR-4708-5p	0.281033806
MIMAT0018065_st	hsa-miR-3646	0.284592893
MIMAT0003240_st	hsa-miR-575	0.303532074
MIMAT0019835_st	hsa-miR-4721	0.306997951
MIMAT0004976_st	hsa-miR-933	0.322809789
MIMAT0006765_st	hsa-miR-1825	0.347249747
MIMAT0017352_st	hsa-miR-2277-5p	0.350295367
MIMAT0004561_st	hsa-miR-187-5p	0.366473454
MIMAT0019068_st	hsa-miR-4529-3p	0.368761744
MIMAT0027431_st	hsa-miR-6765-3p	0.371166068
MIMAT0030430_st	hsa-miR-7855-5p	0.379288897
MIMAT0028117_st	hsa-miR-7110-5p	0.432829251
MIMAT0003270_st	hsa-miR-602	0.460879594
MIMAT0005951_st	hsa-miR-1307-3p	0.465359964
MIMAT0022742_st	hsa-miR-1273g-3p	0.511636188
MIMAT0015052_st	hsa-miR-3175	0.537970962
MIMAT0004614_st	hsa-miR-193a-5p	0.557948308
MIMAT0005867_st	hsa-miR-663b	0.75513205
MIMAT0019745_st	hsa-miR-4668-5p	0.814588736
MIMAT0005939_st	hsa-miR-1281	0.866951101
MIMAT0015055_st	hsa-miR-3178	1.047590393
MIMAT0019069_st	hsa-miR-4530	1.280186233
MIMAT0000421_st	hsa-miR-122-5p	2.12222278

TABLE 11B

Probe Set Name	Transcript ID	log2FC (SNF2 vs. SNF1, 3)
MIMAT0018179_st	hsa-miR-3907	0.172170872
MIMAT0027492_st	hsa-miR-6796-5p	0.180916714
MIMAT0027423_st	hsa-miR-6761-3p	0.181240609
MIMAT0022979_st	hsa-miR-4750-3p	0.191503329
MIMAT0007882_st	hsa-miR-1909-5p	0.223357116
MIMAT0026741_st	hsa-miR-1251-3p	0.258013283
MIMAT0000242_st	hsa-miR-129-5p	0.27251568
MIMAT0015070_st	hsa-miR-3188	0.27589605
MIMAT0019809_st	hsa-miR-4708-5p	0.281033806
MIMAT0018065_st	hsa-miR-3646	0.284592893
MIMAT0003240_st	hsa-miR-575	0.303532074
MIMAT0019835_st	hsa-miR-4721	0.306997951

TABLE 11B-continued

Probe Set Name	Transcript ID	log2FC (SNF2 vs. SNF1, 3)
MIMAT0004976_st	hsa-miR-933	0.322809789
MIMAT0006765_st	hsa-miR-1825	0.347249747
MIMAT0017352_st	hsa-miR-2277-5p	0.350295367
MIMAT0004561_st	hsa-miR-187-5p	0.366473454
MIMAT0019068_st	hsa-miR-4529-3p	0.368761744
MIMAT0027431_st	hsa-miR-6765-3p	0.371166068
MIMAT0030430_st	hsa-miR-7855-5p	0.379288897
MIMAT0028117_st	hsa-miR-7110-5p	0.432829251
MIMAT0003270_st	hsa-miR-602	0.460879594
MIMAT0005951_st	hsa-miR-1307-3p	0.465359964
MIMAT0022742_st	hsa-miR-1273g-3p	0.511636188
MIMAT0015052_st	hsa-miR-3175	0.537970962
MIMAT0004614_st	hsa-miR-193a-5p	0.557948308
MIMAT0005867_st	hsa-miR-663b	0.75513205
MIMAT0019745_st	hsa-miR-4668-5p	0.814588736
MIMAT0005939_st	hsa-miR-1281	0.866951101
MIMAT0015055_st	hsa-miR-3178	1.047590393
MIMAT0019069_st	hsa-miR-4530	1.280186233
MIMAT0000421_st	hsa-miR-122-5p	2.12222278

TABLE 11C

Probe Set Name	Transcript ID	log2FC (SNF2 vs. SNF1, 3)
MIMAT0000418_st	hsa-miR-23b-3p	−0.973911144
MIMAT0000103_st	hsa-miR-106a-5p	−0.940091903
MIMAT0000065_st	hsa-let-7d-5p	−0.855624818
MIMAT0001080_st	hsa-miR-196b-5p	−0.766240429
MIMAT0000264_st	hsa-miR-203a	−0.763078462
MIMAT0000086_st	hsa-miR-29a-3p	−0.735033964
MIMAT0000222_st	hsa-miR-192-5p	−0.714440376
MIMAT0022259_st	hsa-miR-5100	−0.69282742
MIMAT0000066_st	hsa-let-7e-5p	−0.672530325
MIMAT0000259_st	hsa-miR-182-5p	−0.648299131
MIMAT0000093_st	hsa-miR-93-5p	−0.644062486
MIMAT0000318_st	hsa-miR-200b-3p	−0.641440676
MIMAT0000076_st	hsa-miR-21-5p	−0.636319688
MIMAT0000101_st	hsa-miR-103a-3p	−0.635289418
MIMAT0000080_st	hsa-miR-24-3p	−0.599049459
MIMAT0000691_st	hsa-miR-130b-3p	−0.549958054
MIMAT0000278_st	hsa-miR-221-3p	−0.527703234
MIMAT0000243_st	hsa-miR-148a-3p	−0.445186581
MIMAT0000415_st	hsa-let-7i-5p	−0.407014793
MIMAT0000071_st	hsa-miR-17-3p	−0.307974314
MIMAT0001620_st	hsa-miR-200a-5p	−0.260909679
MIMAT0018967_st	hsa-miR-4448	−0.253668944

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1. A method comprising measuring expression levels of one or more genes listed in Table 10A or one or more miRNAs listed in Table 11A in a sample comprising tissue from a metastasis from a primary cancer tumor.

2. The method of claim **1**, wherein the metastasis is a liver metastasis and the primary cancer tumor is a colorectal cancer tumor.

3. (canceled)

4. The method of claim **1**, wherein the expression levels of at least 5 of the genes listed in Table 10A are measured.

5. The method of claim **1**, wherein the expression levels of at least 5 of the miRNAs listed in Table 11A are measured.

6. The method of claim **1**, wherein the expression levels of one or more genes listed in Table 10A and one or more miRNAs listed in Table 11A are measured.

7. (canceled)

8. The method of claim **1**, wherein the expression levels of the one or more genes or one or more miRNAs are within a predetermined amount of a mean expression level in metastases of a cohort of patients having an oligometastatic phenotype, a mean expression level in metastases of a cohort of patients who are likely to be healed without the administration of systemic cancer therapy, or a mean expression level in metastases of a cohort of patients having a mean ten-year overall survival expectation that is at least 60%.

9. The method of claim **8**, wherein the cohort of patients comprises a representative sample of patients having an oligometastatic phenotype.

10. (canceled)

11. The method of claim **1**, wherein:

(A) the expression levels of one or more genes listed in Table 10A or one or more miRNAs listed in Table 11A deviate by a predetermined amount from the mean expression levels of the one or more genes or the one or more miRNAs in metastases of a cohort of metastatic colorectal cancer patients having a mean ten-year overall survival expectation that is less than 50%; or

(b) the expression levels of one or more genes listed in Table 10B are higher by a predetermined amount than the mean expression level of the one or more genes in metastases of said cohort; or

(c) the measured expression levels of one or more genes listed in Table 10C are lower by a predetermined amount than the mean expression level of the one or more genes in metastases of said cohort; or

(d) the measured expression levels of one or more miRNAs listed in Table 11B are higher by a predetermined amount than the mean expression level of the one or more miRNAs in metastases of said cohort; or

(e) the measured expression levels of one or more miRNAs listed in Table 11C are lower by a predetermined amount than the mean expression level of the one or more miRNAs in metastases of said cohort.

12.-**15**. (canceled)

16. The method of claim **11**, wherein said cohort comprises a representative sample of metastatic colorectal cancer patients having a mean ten-year overall survival expectation that is less than 50%.

17. (canceled)

18. The method of claim **1**, further comprising calculating a clinical risk score for the patient.

19.-**22**. (canceled)

24. A method of treating metastatic cancer in a patient, the method comprising administering to the patient a local cancer therapy without administering systemic cancer therapy or administering to the patient an immunotherapy, wherein the patient has been determined to have a metastasis having expression levels of one or more genes listed in Table 10A or one or more miRNAs listed in Table 11B that are within a predetermined amount of the mean expression level of the one or more genes or miRNAs in metastases of a cohort of metastatic cancer patients having a mean overall ten-year survival expectation that is at least 60%.

25. The method of claim **24**, wherein the patient has been determined to have a metastasis having expression levels of at least 5 genes listed in Table 10A and/or at least 5 miRNAs listed in Table 11A that are within a predetermined amount of the mean expression level of the one or more genes or miRNAs in metastases of a cohort of metastatic cancer patients having a mean overall ten-year survival expectation that is at least 60%.

26. The method of claim **24**, wherein the patient has been determined to have an mRNA and/or miRNA expression profile indicating an oligometastatic phenotype based on the expression of one or more genes listed in Table 10A and the expression of one or more genes listed in Table 11A.

27.-**30**. (canceled)

31. The method of, wherein the metastasis is a liver metastasis of a colorectal cancer.

32.-**42**. (canceled)

43. A method comprising evaluating expression levels of multiple mRNA and/or miRNA species in a sample comprising tissue from a liver metastasis of a patient that has metastatic colorectal cancer to identify the patient as belonging to a first group of patients or a second group of patients, wherein:

(a) the first group has one or more of the following characteristics:

(i) a mean ten-year overall survival expectation of at least 60%;

(ii) a mean ten-year overall survival expectation that is higher than that for patients outside of the first group;

(iii) a likelihood of experiencing metastatic recurrence after hepatic resection that is lower than the likelihood for patients outside of the first group;

(iv) a likelihood of being successfully treated without systemic cancer treatments that is higher than the likelihood for patients outside of the first group; and

(v) a likelihood of being successfully treated with immune checkpoint therapy that is higher than the likelihood for patients outside of the first group; and

(b) the second group has one or more of the following characteristics:

(i) a mean ten-year overall survival expectation of less than 50%;

- (ii) a mean ten-year overall survival expectation that is lower than that for patients outside of the second group;
- (iii) a likelihood of experiencing metastatic recurrence after hepatic resection that is higher than for patients outside of the second group;
- (iv) a likelihood of being successfully treated without systemic cancer treatments that is lower than the likelihood for patients outside of the second group;
- (v) a likelihood of being successfully treated with immune checkpoint therapy that is lower than the likelihood for patients outside of the second group; and
- (vi) a likelihood of being successfully treated with DNA damaging cancer therapy that is higher than the likelihood for patients outside of the second group.

44. The method of claim **43**, wherein the expression levels of the multiple mRNA species comprise expression levels of transcripts of one or more genes listed in Table 10A.

45. The method of claim **43**, wherein the expression levels of the multiple miRNA species comprise expression levels of one or more of the miRNAs listed in Table 11A.

46. The method of claim **44**, wherein the patient is identified as belonging to the first group of patients if the expression levels of one or more genes listed in Table 10A is within a predetermined amount of a reference expression level of the one or more genes or if the expression levels of one or more miRNAs listed in Table 11A is within a predetermined amount of a reference expression level of the one or more miRNAs.

47. (canceled)

48. The method of claim **43**, wherein step (b) comprises using a classifier that has been trained to identify an RNA expression pattern associated with the first group of patients, wherein the classifier evaluates the expression levels of at least 5 genes listed in Table 10A and at least 5 of miRNAs listed in Table 11A.

49.-**50**. (canceled)

51. The method of claim **43**, further comprising: (a) administering an immune checkpoint therapy or a local treatment of liver metastases unaccompanied by systemic cancer treatment to a patient identified as belonging to the first group or (b) administering a DNA damaging cancer therapy to a patient identified as belonging to the second group of patients.

52. (canceled)

53. (canceled)

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