A

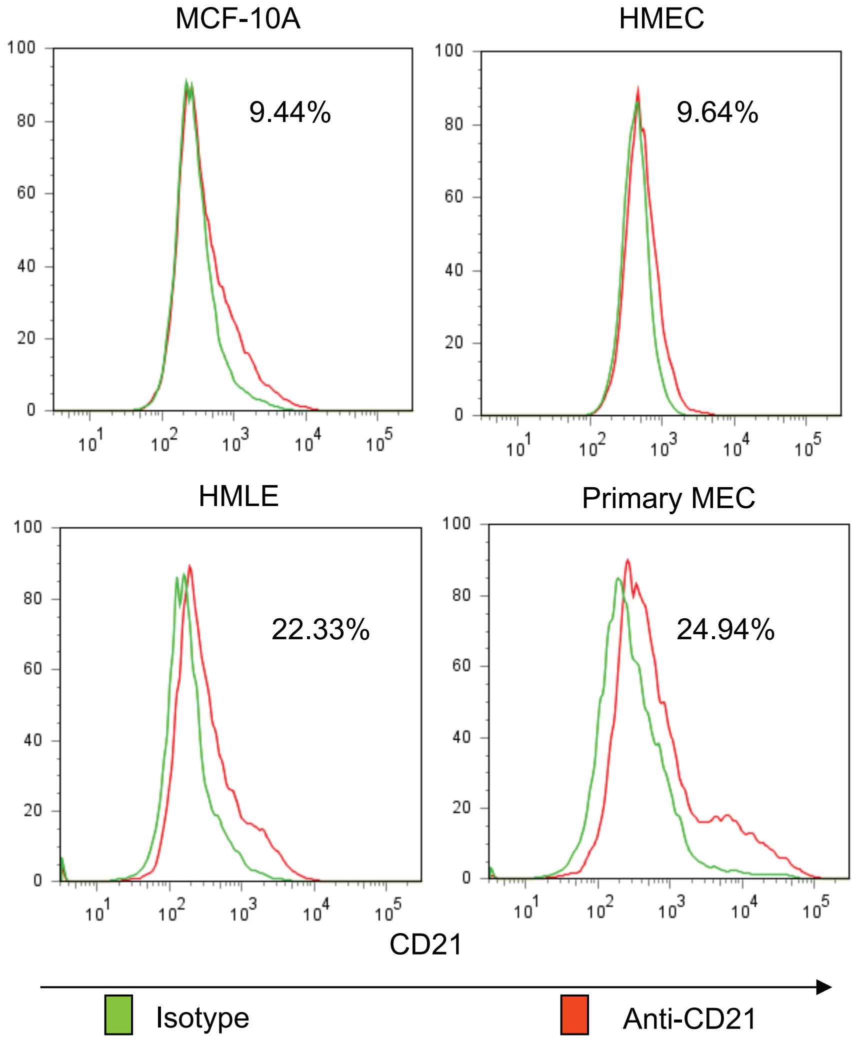

MCF-10A
9.44%
HMEC
9.64%
HMLE
22.33%
Primary MEC
24.94%
100
80
60
40
20
0
10^1
10^2
10^3
10^4
10^5
CD21
🟩 Isotype
🟥 Anti-CD21

Fig.S1

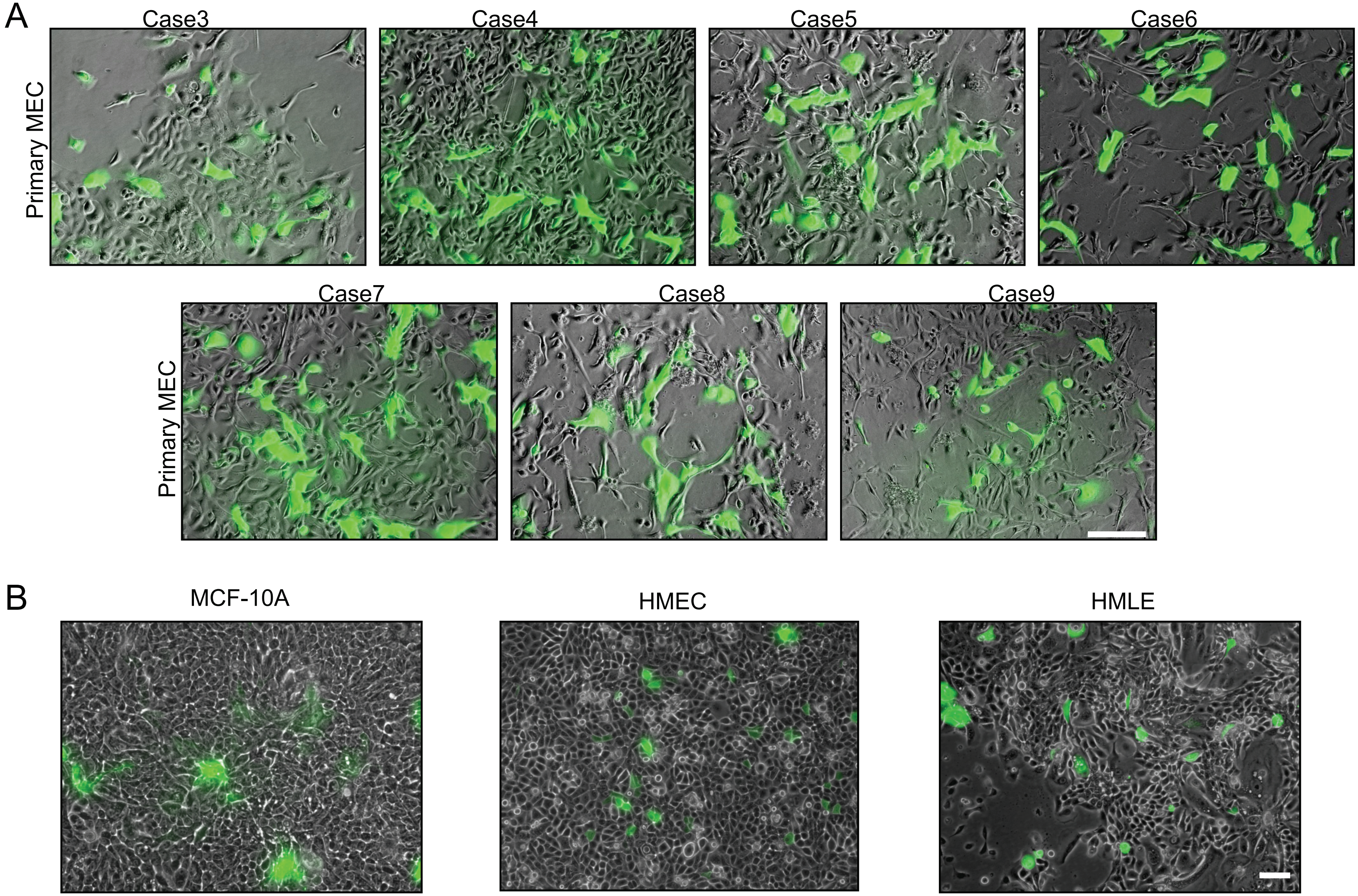

A
Case3
Case4
Case5
Case6
Primary MEC
Case7
Case8
Case9
Primary MEC
B
MCF-10A
HMEC
HMLE

Fig. S2

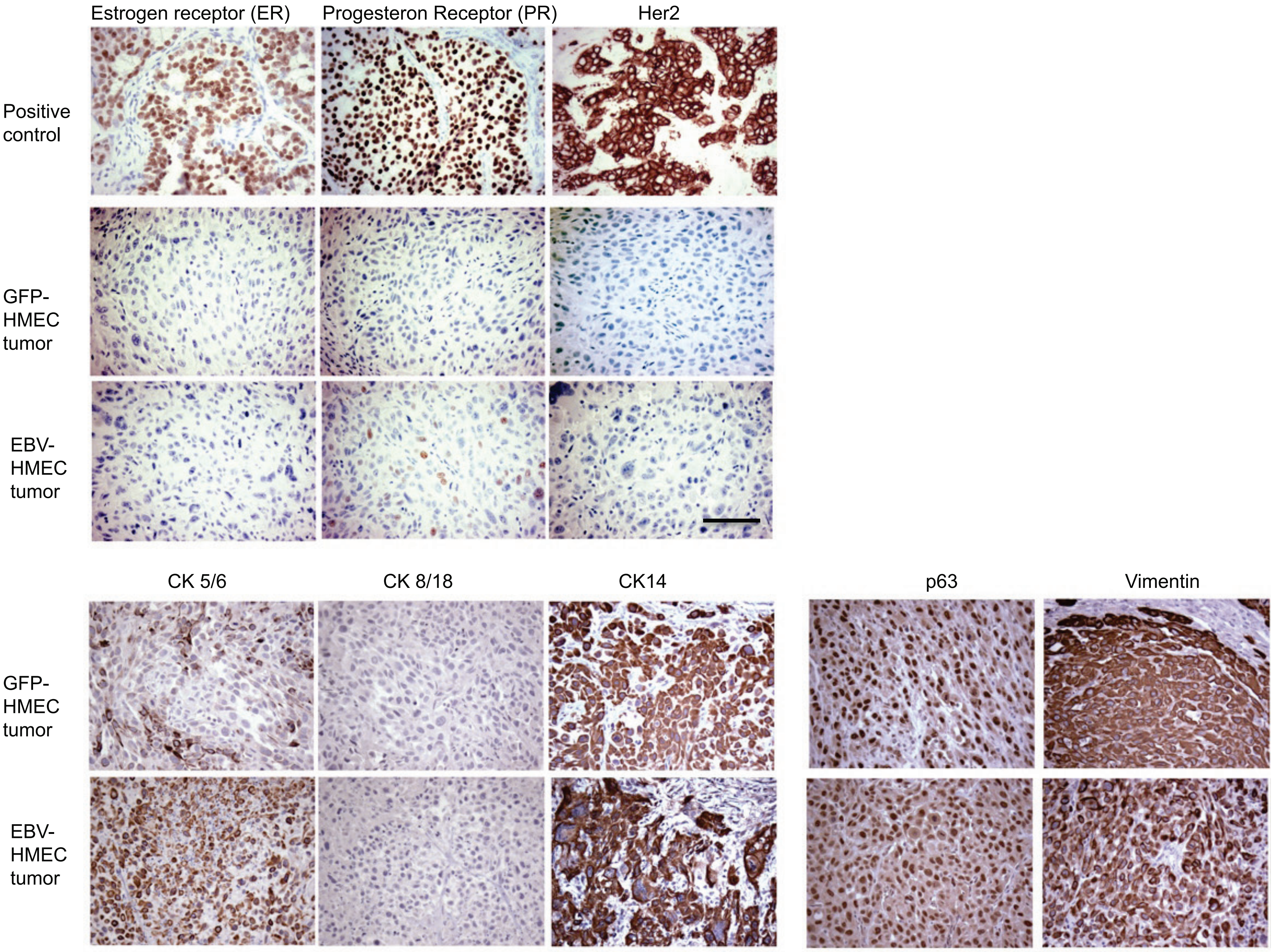

Estrogen receptor (ER)
Progesteron Receptor (PR)
Her2
Positive control
GFP-HMEC tumor
EBV-HMEC tumor
CK 5/6
CK 8/18
CK14
p63
Vimentin
GFP-HMEC tumor
EBV-HMEC tumor

Fig. S 3

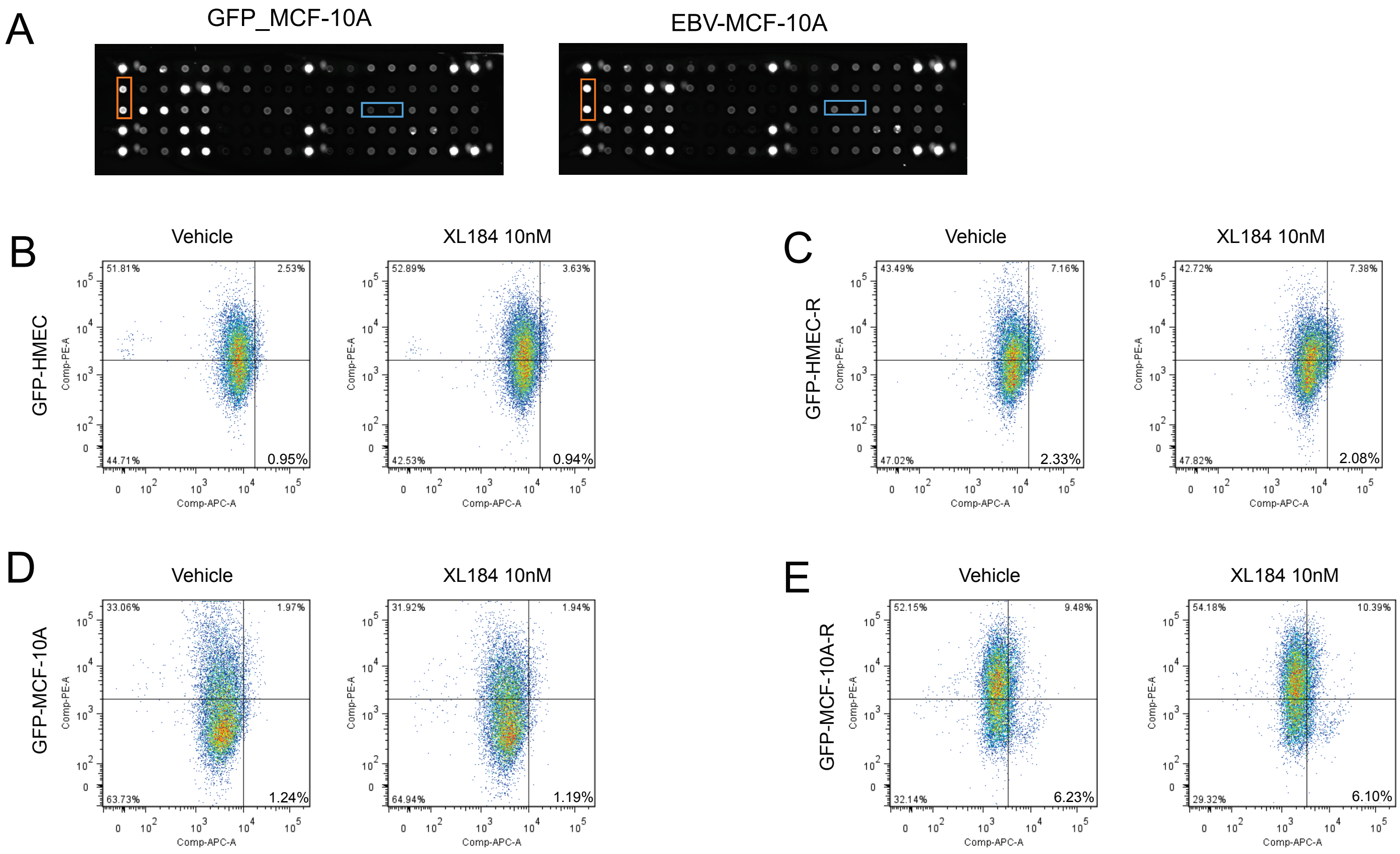

A
GFP_MCF-10A
EBV-MCF-10A
B
Vehicle
XL184 10nM
GFP-HMEC
51.81%
2.53%
44.71%
0.95%
52.89%
3.63%
42.53%
0.94%
C
Vehicle
XL184 10nM
GFP-HMEC-R
43.49%
7.16%
47.02%
2.33%
42.72%
7.38%
47.82%
2.08%
D
Vehicle
XL184 10nM
GFP-MCF-10A
33.06%
1.97%
63.73%
1.24%
31.92%
1.94%
64.94%
1.19%
E
Vehicle
XL184 10nM
GFP-MCF-10A-R
52.15%
9.48%
32.14%
6.23%
54.18%
10.39%
29.32%
6.10%
Comp-PE-A
Comp-APC-A
0
10^2
10^3
10^4
10^5

Fig. S4

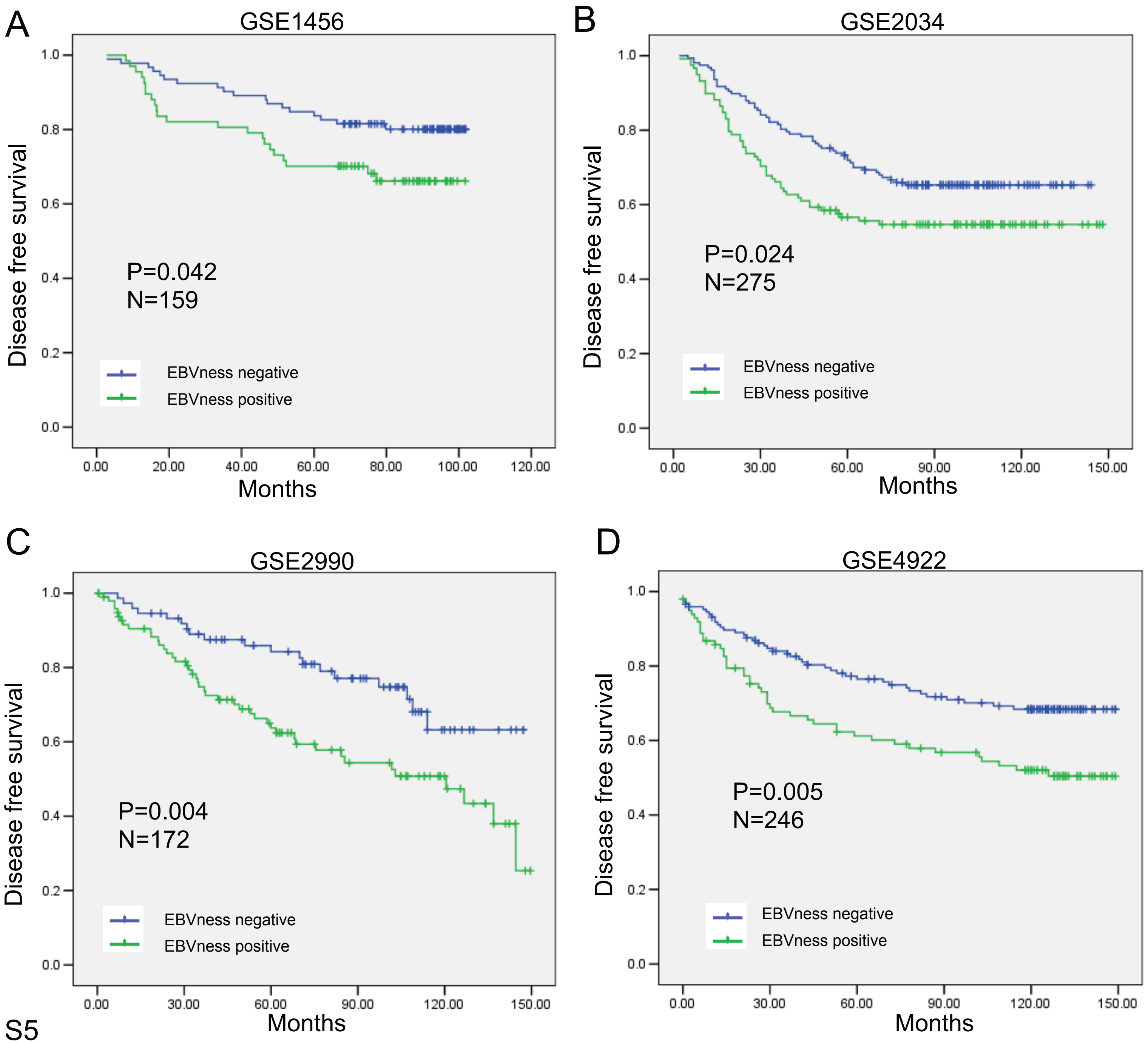

A
GSE1456
Disease free survival
1.0
0.8
0.6
0.4
0.2
0.0
P=0.042
N=159
EBVness negative
EBVness positive
0.00
20.00
40.00
60.00
80.00
100.00
120.00
Months
B
GSE2034
Disease free survival
1.0
0.8
0.6
0.4
0.2
0.0
P=0.024
N=275
EBVness negative
EBVness positive
0.00
30.00
60.00
90.00
120.00
150.00
Months
C
GSE2990
Disease free survival
1.0
0.8
0.6
0.4
0.2
0.0
P=0.004
N=172
EBVness negative
EBVness positive
0.00
30.00
60.00
90.00
120.00
150.00
Months
D
GSE4922
Disease free survival
1.0
0.8
0.6
0.4
0.2
0.0
P=0.005
N=246
EBVness negative
EBVness positive
0.00
30.00
60.00
90.00
120.00
150.00
Months

Fig. S5

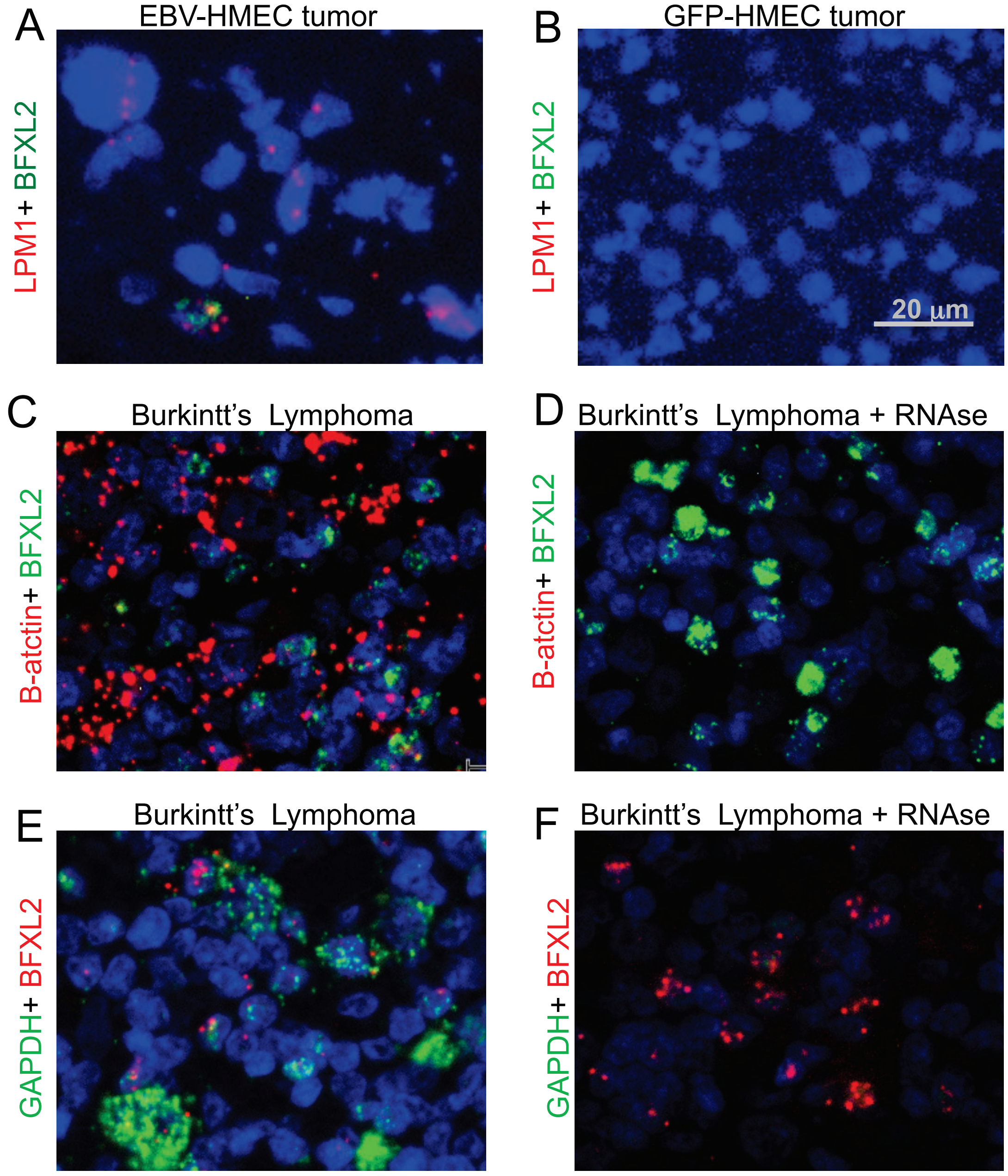
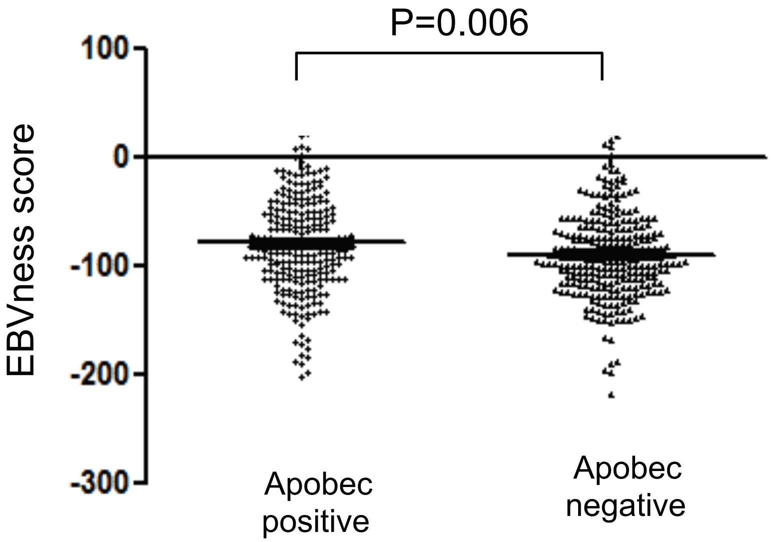

A
EBV-HMEC tumor
LPM1+ BFXL2
B
GFP-HMEC tumor
LPM1+ BFXL2
20 μm
C
Burkintt's Lymphoma
B-atctin+ BFXL2
D
Burkintt's Lymphoma + RNAse
B-atctin+ BFXL2
E
Burkintt's Lymphoma
GAPDH+ BFXL2
F
Burkintt's Lymphoma + RNAse
GAPDH+ BFXL2

Fig. S6

A



B

Apobec	EBVness positive	EBVness negative
Positive	132	117
Negative	113	159

P=0.01

Fig. S7

Table S1

	Symbol	ProbeSet	Fold-change	Parametric p-value	Name
1	ABCE1	201873_PM_s_at	1.61	0.0007744	ATP-binding cassette, sub-family E (OABP), member 1
2	ATAD2	228401_PM_at	1.85	0.0005267	ATPase family, AAA domain containing 2
3	BBS1	218471_PM_s_at	0.57	0.000952	Bardet-Biedl syndrome 1
4	BCCIP	227896_PM_at	2.08	0.0009491	BRCA2 and CDKN1A interacting protein
5	C1orf85	1558693_PM_s_at	0.52	0.0002984	chromosome 1 open reading frame 85
6	C9orf41	228324_PM_at	1.69	0.0001057	chromosome 9 open reading frame 41
7	CBLL1	227187_PM_at	1.45	0.0001082	Cas-Br-M (murine) ecotropic retroviral transforming sequence-like 1
8	CCBE1	242324_PM_x_at	2.08	0.0008049	collagen and calcium binding EGF domains 1
9	CCNC	201955_PM_at	1.89	5.60E-05	cyclin C
10	COMMD10	222637_PM_at	1.85	0.0007051	COMM domain containing 10
11	CPSF2	225994_PM_at	1.69	1.97E-05	cleavage and polyadenylation specific factor 2, 100kDa
12	DDX18	205763_PM_s_at	2.04	1.43E-05	DEAD (Asp-Glu-Ala-Asp) box polypeptide 18
13	c2orf3	216305_PM_s_at	1.69	8.36E-05	chromosome 2 open reading frame 3
14	HCFC1R1	45714_PM_at	0.57	8.41E-05	host cell factor C1 regulator 1 (XPO1 dependent)
15	IDH3A	202070_PM_s_at	1.89	0.0005737	isocitrate dehydrogenase 3 (NAD+) alpha
16	IGFBP2	202718_PM_at	0.16	0.0002672	insulin-like growth factor binding protein 2, 36kDa
17	KIAA1217	1554438_PM_at	1.92	0.0005928	KIAA1217
18	LACTB	1552485_PM_at	1.47	0.0008129	lactamase, beta
19	MALT1	208309_PM_s_at	2.32	0.000812	mucosa associated lymphoid tissue lymphoma translocation gene 1
20	MBD1	208595_PM_s_at	1.82	0.0005863	methyl-CpG binding domain protein 1
21	MBP	1554544_PM_a_at	2.63	0.0006908	myelin basic protein
22	MDP1	228763_PM_at	0.57	0.0004547	magnesium-dependent phosphatase 1
23	ME2	210154_PM_at	4.34	0.0007043	malic enzyme 2, NAD(+)-dependent, mitochondrial
24	MOBKL2B	226844_PM_at	2.85	0.0006736	MOB1, Mps One Binder kinase activator-like 2B (yeast)
25	MYO1B	212365_PM_at	2.04	0.0007291	myosin IB
26	NEDD4	213012_PM_at	2.27	0.000822	neural precursor cell expressed, developmentally down-regulated 4
27	NEDD4L	212445_PM_s_at	3.22	0.0009354	neural precursor cell expressed, developmentally down-regulated 4-like
28	NOL11	221970_PM_s_at	1.67	7.30E-05	nucleolar protein 11
29	PIAS2	1555514_PM_a_at	2	0.0007738	protein inhibitor of activated STAT, 2
30	PIAS3	203035_PM_s_at	0.61	0.0004053	protein inhibitor of activated STAT, 3
31	PSMD12	202352_PM_s_at	1.78	0.0009601	proteasome (prosome, macropain) 26S subunit, non-ATPase, 12
32	RAB3IP	223471_PM_at	1.69	6.74E-05	RAB3A interacting protein (rabin3)
33	RBM26	229433_PM_at	1.69	0.0002696	RNA binding motif protein 26
34	RNF138	218738_PM_s_at	3.33	0.0001565	ring finger protein 138
35	SDC3	202898_PM_at	0.48	0.0004584	syndecan 3
36	SERPINB1	213572_PM_s_at	3.44	0.0003976	serpin peptidase inhibitor, clade B (ovalbumin), member 1
37	SPG20	212526_PM_at	1.54	0.0002159	spastic paraplegia 20 (Troyer syndrome)
38	TNFAIP3	202643_PM_s_at	2.94	0.0007594	tumor necrosis factor, alpha-induced protein 3
39	TP53TG1	210886_PM_x_at	0.56	0.0006349	TP53 target 1 (non-protein coding)
40	UCHL5	219960_PM_s_at	1.92	0.0009459	ubiquitin carboxyl-terminal hydrolase L5
41	USP38	223289_PM_s_at	1.54	0.0006159	ubiquitin specific peptidase 38
42	UTP18	203721_PM_s_at	1.56	0.0001414	UTP18 small subunit (SSU) processome component homolog (yeast)
43	VRK2	205126_PM_at	1.92	0.0008034	vaccinia related kinase 2
44	WRN	205667_PM_at	1.75	0.0005584	Werner syndrome, RecQ helicase-like
45	XPO4	218479_PM_s_at	1.85	0.0007639	exportin 4
46	ZNF165	206683_PM_at	2.22	0.0009119	zinc finger protein 165
47	ZNF503	227195_PM_at	0.47	7.17E-05	zinc finger protein 503

Table S2

	Biocarta Pathway	Pathway description	Number of genes targeted	LS permutation p-value	KS permutation p-value	Efron-Tibshirani's GSA test p-value
1	h_myosinPathway	PKC-catalyzed phosphorylation of inhibitory phosphoprotein of myosin phosphatase	17	0.00008	0.00013	0.01 (+)
2	h_Par1Pathway	Thrombin signaling and protease-activated receptors	27	0.00113	0.00351	0.03 (+)
3	h_igf1mtorpathway	Skeletal muscle hypertrophy is regulated via AKT/ mTOR pathway	30	0.00258	0.00102	0.065 (+)
4	h_ifngPathway	IFN gamma signaling pathway	7	0.00289	0.0136	< 0.005 (+)
5	h_hesPathway	Segmentation Clock	11	0.00819	0.00049	0.01 (-)
6	h_alkPathway	ALK in cardiac myocytes	36	0.00844	0.01833	0.08 (+)
7	h_ps1Pathway	Presenilin action in Notch and Wnt signaling	15	0.00861	0.01808	0.07 (-)
8	h_TPOPathway	TPO Signaling Pathway	24	0.00909	0.03894	0.015 (+)
9	h_vobesityPathway	Visceral Fat Deposits and the Metabolic Syndrome	6	0.01019	0.00554	0.035 (-)
10	h_asbcellPathway	Antigen Dependent B Cell Activation	5	0.01324	0.00069	0.045 (+)
11	h_bbcellPathway	Bystander B Cell Activation	5	0.01324	0.00069	0.045 (+)
12	h_egfPathway	EGF Signaling Pathway	38	0.01355	0.00471	< 0.005 (+)
13	h_metPathway	Signaling of Hepatocyte Growth Factor Receptor	47	0.01955	0.00494	0.015 (+)
14	h_il6Pathway	IL 6 signaling pathway	26	0.02135	0.00749	0.085 (+)
15	h_hSWI-SNFpathway	Chromatin Remodeling by hSWI/SNF ATP-dependent Complexes	16	0.03102	0.00299	0.065 (+)
16	h_pmlPathway	Regulation of transcriptional activity by PML	10	0.04157	0.00508	0.055 (+)
17	h_notchpathway	Proteolysis and Signaling Pathway of Notch	8	0.04249	0.05061	< 0.005 (-)
18	h_appPathway	Generation of amyloid b-peptide by PS1	6	0.04612	0.00858	0.035 (+)
19	h_d4gdiPathway	D4-GDI Signaling Pathway	18	0.05045	0.00952	0.215 (+)
20	h_hsp27Pathway	Stress Induction of HSP Regulation	11	0.0678	0.00945	0.17 (-)
21	h_CCR3Pathway	CCR3 signaling in Eosinophils	17	0.07119	0.00722	0.115 (+)
22	h_il18Pathway	IL 18 Signaling Pathway	5	0.07965	0.00398	0.165 (-)
23	h_atrbrcaPathway	Role of BRCA1, BRCA2 and ATR in Cancer Susceptibility	31	0.11183	0.00737	0.12 (-)
24	h_cytokinePathway	Cytokine Network	6	0.15028	0.00431	0.105 (+)
25	h_cptPathway	Mitochondrial Carnitine Palmitoyltransferase (CPT) System	6	0.17915	0.38451	< 0.005 (-)
26	h_IL12Pathway	IL12 and Stat4 Dependent Signaling Pathway in Th1 Development	10	0.18097	0.05016	< 0.005 (-)
27	h_LairPathway	Cells and Molecules involved in local acute inflammatory response	13	0.20518	0.00933	0.13 (+)
28	h_lympathway	Adhesion and Diapedesis of Lymphocytes	10	0.21319	0.00967	0.14 (+)
29	h_RNApol3Pathway	RNA polymerase III transcription	7	0.31772	0.14816	< 0.005 (-)
30	h_ahspPathway	Hemoglobin@	9	0.38274	0.24416	0.005 (-)
31	h_reckPathway	Inhibition of Matrix Metalloproteinases	13	0.52352	0.38059	< 0.005 (-)
32	h_il3Pathway	IL 3 signaling pathway	7	0.57286	0.88897	< 0.005 (-)
33	h_smPathway	Spliceosomal Assembly	11	0.64876	0.45707	0.005 (-)
34	h_btg2Pathway	BTG family proteins and cell cycle regulation	13	0.84872	0.92699	< 0.005 (-)

Table S3

	Biocarta Pathway	Pathway description	Number of genes targeted	LS permutation p-value	KS permutation p-value	Efron-Tibshirani's GSA test p-value
1	h_ranMSpathway	Role of Ran in mitotic spindle regulation	13	0.00002	0.00001	< 0.005 (+)
2	h_g1Pathway	Cell Cycle: G1/S Check Point	42	0.00016	0.08536	< 0.005 (+)
3	h_cdc25Pathway	cdc25 and chk1 Regulatory Pathway in response to DNA damage	11	0.00032	0.01271	< 0.005 (+)
4	h_ephA4Pathway	Eph Kinases and ephrins support platelet aggregation	12	0.00069	0.00011	< 0.005 (-)
5	h_ranbp2Pathway	Sumoylation by RanBP2 Regulates Transcriptional Repression	14	0.0013	0.20691	< 0.005 (+)
6	h_tgfbPathway	TGF beta signaling pathway	24	0.00133	0.32886	0.03 (+)
7	h_mcmPathway	CDK Regulation of DNA Replication	19	0.0019	0.02509	0.04 (+)
8	h_srcRPTPPathway	Activation of Src by Protein-tyrosine phosphatase alpha	13	0.00523	0.30397	< 0.005 (+)
9	h_asbcellPathway	Antigen Dependent B Cell Activation	5	0.00591	0.02723	< 0.005 (+)
10	h_bbcellPathway	Bystander B Cell Activation	5	0.00591	0.02723	< 0.005 (+)
11	h_rbPathway	RB Tumor Suppressor/Checkpoint Signaling in response to DNA damage	15	0.00623	0.04028	< 0.005 (+)
12	h_smPathway	Spliceosomal Assembly	11	0.00851	0.16987	0.055 (+)
13	h_amiPathway	Acute Myocardial Infarction	12	0.00973	0.22781	< 0.005 (-)
14	h_tob1Pathway	Role of Tob in T-cell activation	11	0.016	0.20903	< 0.005 (+)
15	h_fxrPathway	FXR and LXR Regulation of Cholesterol Metabolism	7	0.01627	0.00075	0.07 (-)
16	h_hsp27Pathway	Stress Induction of HSP Regulation	11	0.01742	0.12518	< 0.005 (+)
17	h_ptc1Pathway	Sonic Hedgehog (SHH) Receptor Ptc1 Regulates cell cycle	10	0.01763	0.19397	< 0.005 (+)
18	h_ace2Pathway	Angiotensin-converting enzyme 2 regulates heart function	6	0.02941	0.55815	< 0.005 (-)
19	h_npp1Pathway	Regulators of Bone Mineralization	6	0.02941	0.55815	< 0.005 (-)
20	h_plateletAppPathway	Platelet Amyloid Precursor Protein Pathway	14	0.03695	0.41662	< 0.005 (-)
21	h_LDLpathway	Low-density lipoprotein (LDL) pathway during atherogenesis	6	0.05778	0.00357	0.095 (-)
22	h_skp2e2fPathway	E2F1 Destruction Pathway	12	0.06228	0.23752	< 0.005 (+)
23	h_akap95Pathway	AKAP95 role in mitosis and chromosome dynamics	13	0.09264	0.25022	0.005 (+)
24	h_intrinsicPathway	Intrinsic Prothrombin Activation Pathway	9	0.09286	0.67113	< 0.005 (-)
25	h_p27Pathway	Regulation of p27 Phosphorylation during Cell Cycle Progression	12	0.09579	0.15707	< 0.005 (+)
26	h_pelp1Pathway	Pelp1 Modulation of Estrogen Receptor Activity	7	0.09669	0.0834	< 0.005 (+)
27	h_ceramidePathway	Ceramide Signaling Pathway	27	0.13267	0.29703	< 0.005 (+)
28	h_vipPathway	Neuropeptides VIP and PACAP inhibit the apoptosis of activated T cells	35	0.14728	0.7075	< 0.005 (-)
29	h_ps1Pathway	Presenilin action in Notch and Wnt signaling	15	0.15846	0.42291	< 0.005 (+)
30	h_stat3Pathway	Stat3 Signaling Pathway	7	0.21504	0.32375	< 0.005 (+)

Table S4

	ProbeSet	Symbol	Name	Weight in Diagonal Linear Discriminant Analysis
1	1554544_PM_a_at	MBP	myelin basic protein	-3.1737
2	1555514_PM_a_at	PIAS2	protein inhibitor of activated STAT, 2	-4.3098
3	201873_PM_s_at	ABCE1	ATP-binding cassette, sub-family E (OABP), member 1	-6.3593
4	201955_PM_at	CCNC	cyclin C	-8.4285
5	202070_PM_s_at	IDH3A	isocitrate dehydrogenase 3 (NAD+) alpha	-5.1207
6	202352_PM_s_at	PSMD12	proteasome (prosome, macropain) 26S subunit, non-ATPase, 12	-4.9795
7	202644_PM_s_at	TNFAIP3	tumor necrosis factor, alpha-induced protein 3	-4.7935
8	202718_PM_at	IGFBP2	insulin-like growth factor binding protein 2, 36kDa	2.0252
9	202898_PM_at	SDC3	syndecan 3	4.6527
10	203035_PM_s_at	PIAS3	protein inhibitor of activated STAT, 3	7.1677
11	203721_PM_s_at	UTP18	UTP18 small subunit (SSU) processome component homolog (yeast)	-10.36
12	205126_PM_at	VRK2	vaccinia related kinase 2	-4.5849
13	205667_PM_at	WRN	Werner syndrome, RecQ helicase-like	-5.7498
14	206683_PM_at	ZNF165	zinc finger protein 165	-3.6134
15	208309_PM_s_at	MALT1	mucosa associated lymphoid tissue lymphoma translocation gene 1	-3.4562
16	208595_PM_s_at	MBD1	methyl-CpG binding domain protein 1	-5.3362
17	208896_PM_at	DDX18	DEAD (Asp-Glu-Ala-Asp) box polypeptide 18	-7.8428
18	210153_PM_s_at	ME2	malic enzyme 2, NAD(+)-dependent, mitochondrial	-2.7999
19	210886_PM_x_at	TP53TG1	TP53 target 1 (non-protein coding)	5.5011
20	212365_PM_at	MYO1B	myosin IB	-4.2106
21	212445_PM_s_at	NEDD4L	neural precursor cell expressed, developmentally down-regulated 4-like	-2.424
22	212526_PM_at	SPG20	spastic paraplegia 20 (Troyer syndrome)	-9.7634
23	213012_PM_at	NEDD4	neural precursor cell expressed, developmentally down-regulated 4	-3.5315
24	213572_PM_s_at	SERPINB1	serpin peptidase inhibitor, clade B (ovalbumin), member 1	-2.7943
25	216305_PM_s_at	C2orf3	GC-rich sequence DNA-binding factor 2	-9.4529
26	218471_PM_s_at	BBS1	Bardet-Biedl syndrome 1	5.1307
27	218479_PM_s_at	XPO4	exportin 4	-4.8683
28	218738_PM_s_at	RNF138	ring finger protein 138	-3.527
29	219960_PM_s_at	UCHL5	ubiquitin carboxyl-terminal hydrolase L5	-4.3732
30	221970_PM_s_at	NOL11	nucleolar protein 11	-10.32
31	222637_PM_at	COMMD10	COMM domain containing 10	-4.9854
32	226844_PM_at	MOBKL2B	MOB kinase activator 3B	-2.9023
33	227187_PM_at	CBLL1	Cas-Br-M (murine) ecotropic retroviral transforming sequence-like 1	-13.986
34	227896_PM_at	BCCIP	BRCA2 and CDKN1A interacting protein	-3.9048
35	228401_PM_at	ATAD2	ATPase family, AAA domain containing 2	-5.4483
36	229433_PM_at	RBM26	RNA binding motif protein 26	-7.4851
37	45714_PM_at	HCFC1R1	host cell factor C1 regulator 1 (XPO1 dependent)	8.9825

Table S5

Character	EBV-like	None-EBV-like	P value
GSE1456			
Basal like tumor	28.6%: (20/70)	5.6% (5/89)	<0.001
GSE2290			
Grade(3)	45.2%(38/84)	15.1% (11/73)	<0.001
Lymph note metastasis (+)	19.1%(18/94)	16.2% (12/74)	0.632
M Stage (1)	55.1% (32/58)	44.7% (38/85)	<0.221
Average tumor size	23.98mm(96)	19.18mm(76)	0.01
ER (-)	25.5%(24/94)	6.8%(5/74)	<0.001
Age	58(96)	56.3(76)	0.313
GSE2034			
M Stage (1)	55.1%(32/58)	44.7% (38/85)	0.221
ER (-)	43.3%(52/120)	13.5%(21/155)	<0.001
GSE4922			
Grade(3)	35.6%(37/104)	12.7% (18/142)	P<0.001
Lymph note metastasis (+)	45.1%(47/104)	28.8%(41/142)	0.008
Average tumor size	23.73mm(96)	21.43mm(76)	0.012
ER (-)	24%(25/104)	9.15%(13/142)	0.001
P53 mutation	37.5% (39/104)	14.9% (21/142)	<0.001
Age(year)	59(104)	64.4(142)	0.005