Supplementary Table 1. Demographics for all study subjects

Supplementary Table 1a. Patient characteristics of the plasma samples obtained on a clinical trial (week 3) consisting of interferon alfa and bortezomib.

Melanoma patients chip 1	12
Sex (n)	
Male	5
Female	7
Age (years)	
Mean	59.8
Median	59
Range	40-82
Tumor extent	Metatastatic
ECOG Performance Status (n)	
0	2
1	8
≥2	1
Unknown	1
% Lysis	33%

Supplementary Table Table 1b. Patient characteristics of the plasma samples obtained from the metastatic melanoma patients utilized for chip 2.

Number of melanoma patients chip 2	9
Sex (n)	
Male	7
Female	2
Age (years)	
Mean	51.7
Median	54
Range	28-66
Tumor extent	Metastatic
ECOG Performance Status (n)	
0	6
1	0
≥2	3
% Lysis	11%

Supplementary Table 1c. Patient characteristics of the plasma samples obtained from the metastatic pancreatic cancer patients utilized for chip 3.

Number of pancreatic adenocarcinoma patients	10
Sex (n)	
Male	8
Female	2
Age (years)	
Mean	62.5
Median	61
Range	49-85
Tumor extent	Metastatic
ECOG Performance Status (n)	
0	2
1	4
≥2	4
% Lysis	20%

Supplementary Table 1d. Patient characteristics of the plasma samples obtained from the normal donor controls utilized for chips 2 and 3.

Number of normal donors	8
Sex (n)	
Male	5
Female	3
Age (years)	
Mean	54.25
Median	55.5
Range	42-64
ECOG Performance Status (n)	
0	8
% Lysis	0%

Supplementary Table 2. Differentially expressed miRNA obtained from the biostatistical analysis.

miRNA	Fold Change	P value
hsa-miR-223-3p	78.31444546	1.02919E-07
hsa-miR-19b-3p	5.777404453	2.18294E-07
hsa-miR-126-3p	16.60968643	3.62074E-07
hsa-miR-23a-3p	11.72551768	4.37262E-07
hsa-miR-130a-3p	8.09982842	7.1817E-07
hsa-let-7b-5p	8.611618329	9.60522E-07
hsa-miR-142-3p	15.14156245	1.83951E-06
hsa-miR-15b-5p	9.321648467	2.0771E-06
hsa-miR-93-5p	7.720855371	2.3533E-06
hsa-let-7g-5p	9.952747709	2.64849E-06
hsa-miR-92a-3p	5.63490397	2.87819E-06
hsa-miR-22-3p	6.20683798	3.34986E-06
hsa-let-7a-5p	14.68266033	3.60255E-06
hsa-miR-199a-3p+hsa-miR-199b-3p	12.20891763	3.9669E-06
hsa-miR-146a-5p	17.7863772	4.19303E-06
hsa-let-7i-5p	10.76293169	4.85896E-06
hsa-miR-191-5p	10.86982455	6.60136E-06
hsa-miR-106a-5p+hsa-miR-17-5p	8.223833947	8.25129E-06
hsa-miR-20a-5p+hsa-miR-20b-5p	8.298595423	1.98462E-05
hsa-miR-423-5p	7.202414489	2.73255E-05
hsa-miR-374a-5p	2.478246674	7.1979E-05
hsa-miR-24-3p	6.049221986	7.22744E-05
hsa-miR-181a-5p	4.891786887	9.93639E-05
hsa-miR-484	3.645089454	0.000105172
hsa-miR-151a-3p	3.111650881	0.00011191
hsa-miR-4454	16.14557335	0.000112769
hsa-miR-631	0.556920222	0.000113117
hsa-miR-19a-3p	3.267187468	0.000173836
hsa-let-7d-5p	5.257483016	0.000198868
hsa-miR-16-5p	5.680377558	0.000209305
hsa-miR-15a-5p	4.043476414	0.00026657
hsa-miR-148a-3p	2.967184544	0.000289513
hsa-miR-361-5p	3.039328937	0.00029006
hsa-miR-221-3p	4.371017407	0.00031459
hsa-miR-1200	0.522062435	0.000412964
hsa-miR-548al	0.447790037	0.000455004
hsa-miR-140-5p	1.593480701	0.000466602
hsa-miR-720	5.768829359	0.000501241
hsa-miR-891a	0.517583099	0.000677765

hsa-miR-26a-5p	3.453952496	0.000678893
hsa-miR-148b-3p	1.867422682	0.000785126
hsa-miR-29a-3p	3.330643042	0.001029677
hsa-miR-1245b-5p	0.570388058	0.001874672
hsa-miR-548n	0.493636078	0.002915744
hsa-miR-188-5p	0.512100462	0.003045036
hsa-miR-328	2.172341194	0.003195606
hsa-miR-548u	0.574072789	0.003304015
hsa-miR-4443	0.452168384	0.003348023
hsa-miR-1183	0.441434486	0.003575194
hsa-miR-155-5p	0.612536829	0.003782074
hsa-miR-197-3p	2.434743175	0.004152169
Chip 2 hsa-miR-494	0.675507	0.00015296
Chip 3 hsa-miR 1245b-3p hsa-miR-1268a	 1.307915 0.729109	 0.000704 0.001415

Supplementary Table 3. Differentially expressed miRNA obtained from the rank-based bioinformatics analysis.

Up-regulated	Down-regulated
Chip 1 hsa-miR-146a-5p hsa-miR-151a-3p hsa-miR-22-3p hsa-let-7a-5p hsa-miR-140-5p hsa-miR-199a-3p+hsa-miR-199b-3p hsa-miR-361-5p hsa-miR-23a-3p hsa-miR-24-3p hsa-miR-29a-3p hsa-miR-106a-5p+hsa-miR-17-5p hsa-let-7i-5p hsa-miR-148a-3p hsa-miR-221-3p hsa-miR-191-5p hsa-let-7d-5p hsa-miR-15b-5p hsa-miR-93-5p hsa-miR-15a-5p hsa-miR-92a-3p hsa-miR-130a-3p hsa-miR-181a-5p hsa-miR-20a-5p+hsa-miR-20b-5p hsa-miR-19b-3p hsa-let-7b-5p hsa-miR-484 hsa-miR-126-3p hsa-miR-423-5p hsa-miR-26a-5p hsa-miR-16-5p hsa-let-7g-5p hsa-let-7d-5p	Chip 1 hsa-miR-548q hsa-miR-548d-3p hsa-miR-4443 hsa-miR-520h hsa-miR-518b hsa-miR-612 hsa-miR-363-3p hsa-miR-631 hsa-miR-548a-5p hsa-miR-888-5p hsa-miR-188-5p hsa-miR-219-5p hsa-miR-1827 hsa-miR-1183 hsa-miR-548al
Chip 2 hsa-miR-16-5p hsa-let-7e-5p hsa-miR-27a-3p	Chip 2 hsa-miR-409-3p
Chip 3 hsa-miR-3127-5p	Chip 3 hsa-miR-1245b-3p

Supplementary Table 4. False positive rates for a chip consisting of 7 patient plasma samples and 4 normal donor controls.

%	Up-regulated	Down- regulated
5	5.09E-07	0.00349169
10	5.25E-05	0.03826375
15	0.00071352	0.1298337
20	0.0041943	0.2684355
25	0.01544952	0.4171371
30	0.0420079	0.5336559
35	0.09187973	0.5885125
40	0.1698693	0.5733089
45	0.2735447	0.4994349
50	0.390625	0.390625
55	0.4994349	0.2735447
60	0.5733089	0.1698693
65	0.5885125	0.09187973
70	0.5336559	0.0420079
75	0.4171371	0.01544952
80	0.2684355	0.0041943
85	0.1298337	0.00071352
90	0.03826375	5.25E-05
95	0.00349169	5.09E-07

Supplementary Table 5. False positive rates for a chip consisting of 8 patient plasma samples and 4 normal donor controls.

	Up-regulated	Down-regulated
5%	2.55E-08	3.32E-03
10%	5.25E-06	3.44E-02
15%	0.000107028	0.1103587
20%	0.000838861	0.2147484
25%	0.003862381	0.3128529
30%	0.01260237	0.3735591
35%	0.03215791	0.3825331
40%	0.06794772	0.3439854
45%	0.1230951	0.2746892
50%	0.1953125	0.1953125
55%	0.2746892	0.1230951
60%	0.3439854	0.06794772
65%	0.3825331	0.03215791
70%	0.3735591	0.01260237
75%	0.3128529	0.003862381
80%	0.2147484	0.000838861
85%	0.1103587	0.000107028
90%	0.03443738	5.25E-06
95%	0.003317102	2.55E-08

Supplementary Table 6. Principal Component analysis

Chip	Eigenvalue of Component 1	Eigenvalue of Component 2	Eigenvalue of Component 3	Eigenvalue of Component 4
1	8.2249 (68.5%)	2.8476 (23.7%)	0.6664 (5.5%)	0.1294 (1.1%)
2	8.1588 (74.2%)	2.4666 (22.4%)	0.1814 (1.6%)	0.0705 (0.6%)
3	9.6334 (80.3%)	1.2394 (10.3%)	0.6711 (5.6%)	0.3299 (2.7%)

Supplementary Table 7. Table of significant miRNAs in melanoma.

miRNA	Function in melanoma	Reference
Let-7a	Let-7a leads to downregulation of integrin beta-3; Loss of let-7a expression leads to progression of melanoma	1
Let-7b	Inhibits anchorage-independent growth of melanoma cells	2
Let-7b	Suppresses BSG expression, melanoma growth and metastasis	3
Let-7b	Increases radiosensitivity of uveal melanoma	4
miR-7-5p	Inhibits melanoma cell invasiveness	5
miR-21	Oncogenic miRNA	6
miR-21	TIMP3 inhibition; increases invasiveness of melanoma	7
miR-21	Oncogenic	8
miR-21	Oncogenic; redistributes PTEN to the nucleus	9
miR-21	Associated with melanoma tumor burden	10
miR-21	Inhibits FBXO11; promotes cell proliferation	11
miR-21	Promotes metastasis	12
miR-21	Negative prognostic factor for patient survival	13
miR-21	Upregulated in melanoma; decreases apoptosis	14
miR-34a	Targets FLOT2; inhibits WM451melanoma cell proliferation	15
miR-34a	Downregulates c-Met; decreases uveal melanoma proliferation	16
miR-34a	Increases apoptosis, inhibits survivin	17
miR-34a	Role in late tumorigenesis; does not appear to be the driver for inherited melanoma	18
miR-34a	Downregulated in melanoma	19
miR-34a	Reduced tumor growth	20
miR-34a	Tumor suppressor gene	21
miR-34b/c	Suppresses uveal melanoma	22
miR-34a/b/c	Suppresses metastasis	23
miR-34b	Expression leads to reduced invasiveness of A375 and WM1552C cell lines	24
miR-125b	Targets MLK3; inhibits cell proliferation	25
miR-125b	Induces senescence	26
miR-125b	Downregulated in lesions with early metastasis	27
miR-125b	Expression is reduced in melanoma	28
miRNA	Decreases melanoma progression	29
miR-125b	Increased in metastatic melanoma; lower patient survival	30
miR-125b	Induces senescence in melanoma	31
miR-125b	Diminishes pigmentation genes and melanin	32
miR-137	Downregulates MITF and CDK6 and serves as a tumor suppressor in uveal melanoma	33
miR-137	Targets PAK2; inhibits cell proliferation	34
miR-137	Targets micropthalmia-associated transcription factor in melanoma cell lines	35

miR-137	Targets CtBP1, inhibits epithelial mesenchymal transition and induces apoptosis	36
miR-137	Downregulates oncogenes	37
miR-137	Targets steroid receptor co activators SRC1, SRC2, and SRC3 in uveal melanoma; inhibits cell proliferation	38
miR-146a	Plays a role in melanoma pathogenesis	39
miR-146a	Enhances tumor growth; decreases metastasis	40
miR-146a	Activates Notch signaling and promotes progression of melanoma	41
miR146a	Prognostic marker for metastasis	42
miR-146a	Suppresses metastatic brain tumors	43
miR-155	Loss of this miRNA enhances MDSC function and enhances melanoma cell proliferation	44
miR-155	Targets SKI; enhances melanoma proliferation	45
miR-155	Pro-apoptosis	46
miR-155	Enables immune escape	47
miR-155	Enhances cell proliferation via MDSC	48
miR-193b	Associated with poor melanoma survival	49
miR-193b	Downregulation leads to increased STMN1 and subsequently promotes proliferation and migration of melanoma cells	50
miR-193b	Suppress cell proliferation and regulates cyclin D1 in melanoma	51
miR-193b	Downregulation of miR-193b leads to melanoma progression; Regulates mcl-1;	52
miR-200	Expressed in melanoma; associated with different mechanisms of invasion	53
miR-200c	Inhibits melanoma growth and metastasis in murine model	54
miR-200c	Plays a role in BRAF inhibitor resistant melanoma	55
miR-200c	Expression in $CD44^{+}CD133^{+}$ cells leads to decreased tumor growth	56
miR-200c	Downregulated in melanoma cell lines and patient samples	57
miR-200c	Downregulates BMI-1; inhibits melanoma proliferation	58
miR-203	Anti-oncogenic; Targets kinesin superfamily protein 5b; regulates melanosome transport	59
miR-203	A lower expression of this miRNA is associated with a short survival time of patients.	60
miR-203	Targets E2F3, induces senescence in melanoma cells	61
miR-203	Targets polycomb group gene BMI1; inhibits invasiveness of melanoma	62
miR-205	Loss of miRNA-205 is associated with melanoma progression	63
miR-205	Inhibitory effect on bcl-2, ABCA2, ABCA5	64
miR-205	Tumor suppressor miRNA	65
miR-205	Regulates E2F1 and suppresses melanoma proliferation	66
miR-205-5p	Curcumin treated melanoma upregulated miR-205-5p; bcl-2 was downregulated in these tumors	67

miR-210	Promotes immune escape from cytotoxic T lymphocytes	68
miR-210	Expression leads to enhances MDSC activity; enhances tumor growth	69
miR-210	Plasma levels are an indicator of recurrence	70
miR-210	Transcriptional regulation; repressor of Myc	71
miR-210	Downregulation leads to resistance to MEK inhibitors	72
miR-210	Upregulated in brain metastasis	73
miR-211	Inversely correlated with melanoma bulk	74
miR-211	Regulator of KCNMA1 expression; reduces melanoma invasion	75
miR-211	Downregulation of this miRNA leads to reduced PRAME protein in melanoma	76
miR-211	Associated with increased levels of bcl-2	77
miR-211	Expression is decreased in melanoma cells	78
miR-211	Targets micropthalmia-associated transcription factor; associated with melanoma invasion	79
miR-211	Tumor suppressor	80
miR-211	Reduces TGF-beta (TGF-beta plays a role in melanocyte stem cell function)	81
miR-211	Downregulation associated with malignant melanoma versus normal nevi.	82
miR-221	Predictor of poor 5 year survival	83
miR-221	Serum levels increased in melanoma patients	84
miR-221	Tumor marker for melanoma	85
miR-221	Inhibits cKit, p27	86
miR-221	Melanoma cells treated with interferon-beta led to downregulation of miR-221 and subsequent upregulation of p27	87

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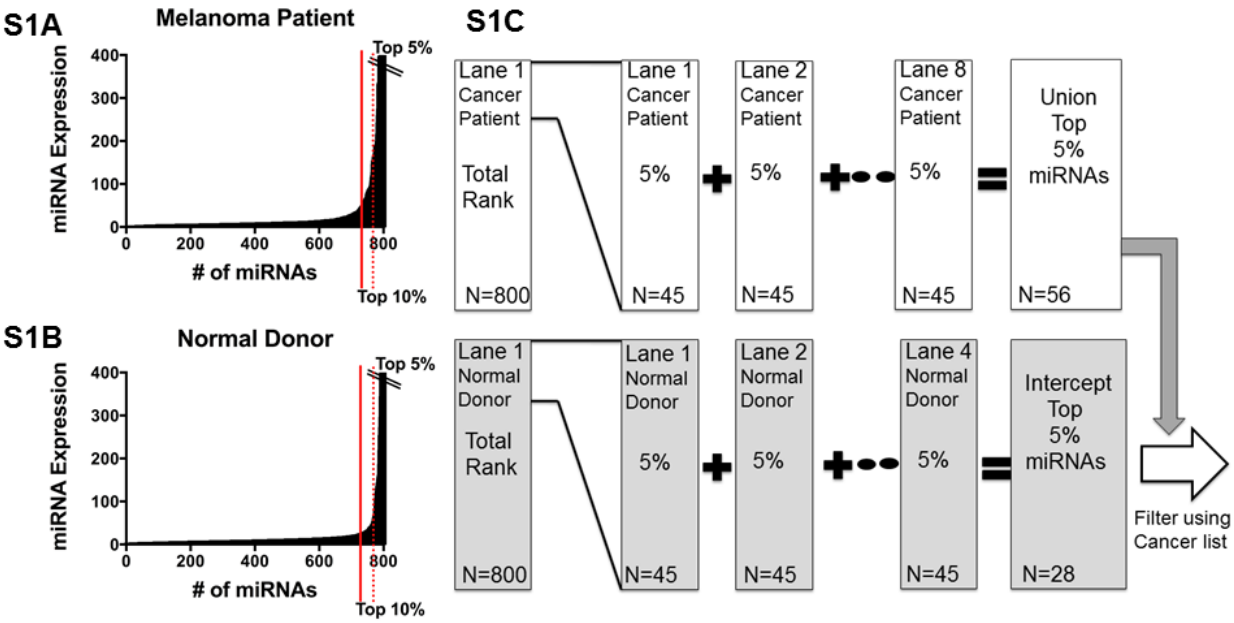
Supplementary Figure 1.



The process for selecting down-regulated miRNAs is illustrated for chip 1. First, the 800 miRNAs identified by NanoString in each lane (one lane per patient) were ordered from highest to lowest expression (**ranked**). S1A) A list of the top 5% (45) of the miRNAs present in the plasma of a cancer patient in chip 1 was generated. S1B) A list of the top 5% (45) of the miRNAs that were present in the plasma of the first normal control donor was generated. S1C) The process is repeated for each of the 8 patient samples and 4 normal donors, and thus 12 such lists were created. The miRNAs that were present in any of the top 5% of the patient lists (8 lists, N = 56; union of the patient lists) were removed from the miRNAs that were present in the top 5% of highly expressing miRNAs in all the normal donor lists (8 lists, N = 28; intercept of the normal donor lists) to generate a list consisting of 15 down-regulated miRNAs in patient samples. Our rank-based method starts the selection of down-regulated miRNAs in a convenient feature list size of the top 5% of miRNAs and repeats the process of finding down-regulated miRNAs by expanding the feature list size (by 5%) through multiple iterations until the

most number of down-regulated miRNAs are selected that have a nonrandom false positive rate. For the first chip, this cut off is 5% with a false positive rate < 0.01. A similar process was utilized to obtain the up-regulated miRNAs in the melanoma and pancreatic cancer tumor bank cohorts.