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Supplemental materials

	No.	Sex	Age	Primary Site	Metastasis
AS	10	M	66	Head	Neck LN
	11	F	78	Unknown	Bone, Muscle
	12	M	85	Head	-
	13	M	89	Head	Lung, Liver
	14	M	81	Leg	LN
	15	F	95	Head	-
MM	1	M	101	Plantar	Liver, LN (Stage IV)
	2	M	75	Chest	Adrenal gland, Lung, LN (Stage IV)
	3	M	61	Chest	LN (Stage IIIc)
	4	F	51	Unknown	Bone, LN (Stage IV)
	5	F	54	Labia majora	LN (Stage IIIc)
	6	F	71	Chest	LN (Stage IIIc)
HC	1	F	93		
	2	F	82		
	3	F	73		
	4	F	69		
	5	M	69		
	6	F	64		

Supplemental Table 1. Patients profile of the serum samples for quantitative reverse transcription PCR (qRT-PCR) using TaqMan MicroRNA Assay performed for comparison with malignant melanoma (MM) patients and healthy controls (HCs).

Four of the six angiosarcoma patients had lymph node or distant metastases. Six MM patients were with advanced stages including Stage IIIc or Stage IV according to AJCC 8th edition. Six HCs had no history of malignancy. Patients AS10-AS15 are the same patients who underwent miRNA microarray analysis shown in Figure1a. LN: Lymph node.

	No.	Sex	Age	Primary Site	Metastasis	Intervals (Months)
AS	6	M	84	Head	LN's	8
	15	F	95	Head	-	27
	16	M	76	Head	LN's	2

Supplemental Table 2. Profile of the serum samples of cutaneous angiosarcoma (AS) patients for quantitative reverse transcription PCR (qRT-PCR) using TaqMan MicroRNA Assay performed for comparison between the time of initial diagnosis and advanced stage. Serum extracellular vesicle-associated microRNAs (EV-miRNAs) of three AS patients were analyzed by qRT-PCR. AS6 and AS15 are the same patients who underwent miRNA microarray analysis. LN: Lymph node.

Regulation	Top Genes	Log2 FC	FDR (Padj)
Up	HSA-MIR-5093	4.21902751	3.88E-08
Up	HSA-MIR-3926	4.144791991	7.32E-07
Up	HSA-MIR-5703	2.938197119	1.19E-08
Up	HSA-MIR-1910-3P	2.741577096	0.000107332
Up	HSA-MIR-3925-5P	2.696481027	2.07E-07
Up	HSA-MIR-6876-5P	2.68295175	1.26E-09
Up	HSA-MIR-296-3P	2.572232225	1.06E-09
Up	HSA-MIR-6859-5P	2.509660726	0.000897039
Up	HSA-MIR-6892-5P	2.431458735	8.46E-08
Up	HSA-MIR-3144-5P	2.327998354	3.83E-09
Up	HSA-MIR-6828-5P	2.319655602	9.36E-07
Up	HSA-MIR-184	2.29209011	3.88E-07
Up	HSA-MIR-12128	2.251865851	5.41E-07
Up	HSA-MIR-8060	2.228765625	1.17E-06
Up	HSA-MIR-3186-3P	2.23869347	3.00E-06
Up	HSA-MIR-4436B-3P	2.118938878	0.001872819
Up	HSA-MIR-4538	2.05256844	2.55E-07
Up	HSA-MIR-6728-5P	1.994959057	0.00242339
Up	HSA-MIR-12117	1.981148878	1.87E-05
Up	HSA-MIR-593-5P	1.979175407	0.000172194
Up	HSA-MIR-6501-3P	1.97441312	0.00071897
Up	HSA-MIR-4635	1.919892314	0.034545462
Up	HSA-MIR-3616-3P	1.784422496	8.81E-08
Up	HSA-MIR-6750-5P	1.772475806	1.66E-05
Up	HSA-MIR-4440	1.673383136	2.69E-05
Up	HSA-MIR-4499	1.660086964	8.46E-08
Up	HSA-MIR-3158-5P	1.623215564	5.89E-08
Up	HSA-MIR-6807-5P	1.612913139	6.88E-07
Up	HSA-MIR-5911	1.601658873	5.89E-08
Up	HSA-MIR-6717-5P	1.543207903	0.002070889
Up	HSA-MIR-3131	1.467534453	9.13E-06
Up	HSA-MIR-4259	1.464877035	0.003378334
Up	HSA-MIR-4496	1.441663734	2.81E-06
Up	HSA-MIR-3126-5P	1.4299273	2.53E-05
Up	HSA-MIR-4322	1.429670488	0.00015067
Up	HSA-MIR-320B	1.419771694	7.01E-05
Up	HSA-MIR-4800-5P	1.405791933	1.46E-06
Up	HSA-MIR-6736-5P	1.375490131	4.45E-05
Up	HSA-MIR-518C-5P	1.372110078	1.37E-05
Up	HSA-MIR-642A-3P	1.362801125	1.34E-05
Up	HSA-MIR-4727-3P	1.356261027	0.000114151
Up	HSA-MIR-4751	1.300519051	2.31E-05
Up	HSA-MIR-4462	1.299750362	1.63E-05
Up	HSA-MIR-12119	1.296323507	2.90E-05
Up	HSA-MIR-3124-5P	1.295599182	1.43E-05
Up	HSA-MIR-6830-5P	1.286208631	8.04E-06
Up	HSA-MIR-3153	1.282349196	0.000396953
Up	HSA-MIR-3682-3P	1.26516015	0.054852205
Up	HSA-MIR-6822-5P	1.264136717	0.006268874
Up	HSA-MIR-320A-3P	1.245502397	4.98E-05
Up	HSA-MIR-4506	1.239354766	0.00022285
Up	HSA-MIR-4654	1.238954944	0.000262739
Up	HSA-MIR-6812-5P	1.226675912	3.33E-06
Up	HSA-MIR-514B-5P	1.223419489	3.33E-06
Up	HSA-MIR-6846-5P	1.222106416	0.000108911
Up	HSA-MIR-4300	1.201366579	0.000121854
Up	HSA-MIR-668-5P	1.19942599	0.002141448
Up	HSA-MIR-4489	1.195347663	0.003898011

Regulation	Top Genes	Log2 FC	FDR (Padj)
Up	HSA-MIR-4747-5P	1.1923786461	2.55E-05
Up	HSA-MIR-3928-3P	1.183818142	1.43E-06
Up	HSA-MIR-671-5P	1.17285359	0.000104839
Up	HSA-MIR-6835-5P	1.152659776	0.000997139
Up	HSA-MIR-765	1.146636892	0.002857039
Up	HSA-MIR-6511B-5P	1.137054816	0.000869524
Up	HSA-MIR-4793-5P	1.133358055	0.014504121
Up	HSA-MIR-4726-5P	1.114105545	1.37E-05
Up	HSA-MIR-1185-2-3P	1.105660756	1.51E-05
Up	HSA-MIR-9718	1.096960004	0.00022739
Up	HSA-MIR-6753-5P	1.076015856	0.007468652
Up	HSA-MIR-6709B-5P	1.073071134	3.94E-05
Up	HSA-MIR-12116	1.065996448	1.51E-05
Up	HSA-MIR-3610	1.047578626	0.000359094
Up	HSA-MIR-3151-5P	1.029117375	0.000363107
Down	HSA-MIR-125B-1-3P	-3.542464754	2.92E-07
Down	HSA-MIR-125A-3P	-2.723169359	1.55E-08
Down	HSA-MIR-6801-3P	-2.661247339	4.04E-10
Down	HSA-MIR-887-5P	-2.350663901	5.89E-08
Down	HSA-MIR-204-3P	-2.28258065	0.00064209
Down	HSA-MIR-6126	-2.272308298	1.43E-06
Down	HSA-MIR-449B-3P	-2.134175507	5.67E-08
Down	HSA-MIR-4648	-2.116190177	0.000759448
Down	HSA-MIR-575	-2.054307162	5.81E-06
Down	HSA-MIR-3937	-1.878414947	6.93E-05
Down	HSA-MIR-6727-5P	-1.842786485	2.52E-05
Down	HSA-MIR-7851-3P	-1.837526923	2.20E-05
Down	HSA-MIR-7113-5P	-1.790637486	0.009588923
Down	HSA-MIR-4497	-1.769709025	0.000549171
Down	HSA-MIR-7704	-1.766016996	6.93E-05
Down	HSA-MIR-6798-5P	-1.747387179	1.18E-06
Down	HSA-MIR-4467	-1.707972963	4.99E-05
Down	HSA-MIR-10400-3P	-1.698183419	9.74E-08
Down	HSA-MIR-12136	-1.691812947	0.014056798
Down	HSA-MIR-23A-3P	-1.667249425	0.071092297
Down	HSA-MIR-4281	-1.647902952	1.22E-05
Down	HSA-MIR-8069	-1.58965871	2.85E-05
Down	HSA-MIR-223-3P	-1.583608227	0.016036634
Down	HSA-MIR-3196	-1.573891583	2.96E-05
Down	HSA-MIR-3960	-1.570286953	2.22E-05
Down	HSA-MIR-10396B-5P	-1.566100701	1.43E-05
Down	HSA-MIR-4787-5P	-1.557952141	1.53E-05
Down	HSA-MIR-2861	-1.55736023	4.98E-05
Down	HSA-MIR-10400-5P	-1.549727813	3.49E-05
Down	HSA-MIR-4466	-1.539135259	1.87E-05
Down	HSA-MIR-6089	-1.528475042	6.58E-06
Down	HSA-MIR-4734	-1.526654195	2.34E-05
Down	HSA-MIR-887-3P	-1.50621333	1.16E-05
Down	HSA-MIR-4530	-1.506025011	6.14E-05
Down	HSA-MIR-6820-5P	-1.50368539	0.000337306
Down	HSA-MIR-6090	-1.496198751	6.64E-06
Down	HSA-MIR-6724-5P	-1.491043007	9.15E-07
Down	HSA-MIR-10392-5P	-1.485544603	9.55E-07
Down	HSA-MIR-4634	-1.484430505	4.45E-05
Down	HSA-MIR-1915-3P	-1.48268037	2.34E-05
Down	HSA-MIR-1268A	-1.479956284	3.17E-05
Down	HSA-MIR-551B-5P	-1.47756704	0.000337306
Down	HSA-MIR-3178	-1.477445576	4.98E-05

Regulation	Top Genes	Log2 FC	FDR (Padj)
Down	HSA-MIR-6784-5P	-1.466958086	0.000071608
Down	HSA-MIR-4488	-1.45672494	1.60E-05
Down	HSA-MIR-10401-3P	-1.446490709	0.002388346
Down	HSA-MIR-1237-5P	-1.421107085	3.03E-05
Down	HSA-MIR-4486	-1.421037498	6.93E-05
Down	HSA-MIR-1908-5P	-1.416168198	1.43E-05
Down	HSA-MIR-4651	-1.406267484	1.27E-05
Down	HSA-MIR-4674	-1.398971353	0.000484539
Down	HSA-MIR-6780B-5P	-1.391206062	3.18E-05
Down	HSA-MIR-638	-1.382520726	3.46E-06
Down	HSA-MIR-6786-5P	-1.37615297	8.33E-05
Down	HSA-MIR-10527-5P	-1.365191411	0.002658915
Down	HSA-MIR-3184-5P	-1.364772956	0.000944759
Down	HSA-MIR-6726-5P	-1.361439989	0.000229402
Down	HSA-MIR-6789-5P	-1.359997488	1.43E-05
Down	HSA-MIR-3665	-1.329071827	6.55E-05
Down	HSA-MIR-7108-5P	-1.327439474	3.86E-05
Down	HSA-MIR-10396A-5P	-1.326502988	4.98E-05
Down	HSA-MIR-6791-5P	-1.32503514	2.34E-05
Down	HSA-MIR-4476	-1.323967296	0.01347493
Down	HSA-MIR-10392-3P	-1.322919949	0.00012236
Down	HSA-MIR-4508	-1.310059576	4.98E-05
Down	HSA-MIR-3940-5P	-1.303678795	0.000273999
Down	HSA-MIR-4741	-1.293879622	8.18E-05
Down	HSA-MIR-8072	-1.284252759	1.00E-05
Down	HSA-MIR-1268B	-1.280426162	4.89E-05
Down	HSA-MIR-6816-5P	-1.260353691	5.69E-05
Down	HSA-MIR-6850-5P	-1.257975348	4.99E-05
Down	HSA-MIR-744-5P	-1.255622317	0.000316527
Down	HSA-MIR-6132	-1.238503049	0.000309014
Down	HSA-MIR-1909-3P	-1.234040302	0.000273999
Down	HSA-MIR-6813-5P	-1.218599981	1.22E-05
Down	HSA-MIR-6125	-1.214814033	2.90E-05
Down	HSA-MIR-6729-5P	-1.214307792	2.62E-05
Down	HSA-MIR-4492	-1.207730295	0.000359094
Down	HSA-MIR-762	-1.204701009	0.000385183
Down	HSA-MIR-4253	-1.194677746	0.01102976
Down	HSA-MIR-4745-5P	-1.17989781	0.006787795
Down	HSA-MIR-1207-5P	-1.176085487	2.52E-05
Down	HSA-MIR-6778-5P	-1.175940553	0.03082527
Down	HSA-MIR-4484	-1.17586773	0.000431006
Down	HSA-MIR-486-3P	-1.17014408	0.000528709
Down	HSA-MIR-1908-3P	-1.168136101	4.99E-05
Down	HSA-MIR-6805-5P	-1.161486472	0.000120934
Down	HSA-MIR-6869-5P	-1.16078418	0.000944759
Down	HSA-MIR-4327	-1.155125026	0.000115282
Down	HSA-MIR-6836-3P	-1.137190763	2.55E-05
Down	HSA-MIR-328-5P	-1.13273123	0.00037686
Down	HSA-MIR-3663-3P	-1.129422164	0.000845981
Down	HSA-MIR-6803-5P	-1.112407501	0.000104839
Down	HSA-MIR-6821-5P	-1.094168583	4.98E-05
Down	HSA-MIR-1203	-1.091849302	0.00744485
Down	HSA-MIR-663B	-1.089204457	0.001230353
Down	HSA-MIR-3679-5P	-1.089135208	0.001170144
Down	HSA-MIR-6752-5P	-1.077212242	3.86E-05
Down	HSA-MIR-5100	-1.073541915	0.034341286
Down	HSA-MIR-6088	-1.015639984	4.13E-05

Supplemental Table 3. The results of differential expression analysis of miRNA microarray analysis. 73 differentially upregulated genes and 100 differentially downregulated genes were identified.

Skin Malignancies	Upregulated miRNAs		Downregulated miRNAs	
	Serum	Plasma	Serum	Plasma
Malignant Melanoma	miR-532-5p, miR-106b1 (23) miR-191, let-7a (26) miR-494 (27)	miR-17, miR-19a, miR-21, miR-126, miR-149 (24) in thicker melanoma Clark level III, IV and V	miR-125b (25)	miR-17, miR-19a, miR-21, miR-126, miR-149 (24) in thinner melanoma Clark level I/II

Supplemental Table 4. Previously reported extracellular vesicle-associated microRNAs (EV-miRNAs) associated with skin malignancies. Only miRNAs associated malignant melanoma were reported. Parentheses are used to indicate the reference numbers.