

Supplementary Figure Legends

Figure S1. Tumor cells stimulate endothelial miRNAs. A. Verification of tumor-induced miRNAs by quantitative RT-PCR in brain endothelial cells co-cultured with SF539, colon endothelial cells co-cultured with HM7 and pancreas endothelial cells co-cultured with Panc1 for 24 hours. * $p < 0.05$, Student's t-test. B. Induction of miRNAs in lung endothelial cells by a panel of NSCLC lines. C. Quantitative RT-PCR of miRNA expression in HUVECs co-cultured with different tumor cell lines. * $p < 0.05$, Student's t-test.

Figure S2. Tumor conditioned media induces miRNAs. A. Quantitative RT-PCR of miRNA expression in endothelial cells stimulated with tumor conditioned medium for 24 hours. * $p < 0.05$, Student's t-test. B. Effects of different angiogenic factors on endothelial miRNA expression. C. Tumor conditioned medium was concentrated with Amicon centrifugal filters as indicated. Both retentates and diffusates were tested for the ability to induce endothelial miRNAs. D. Quantitative PCR of miRNAs in skin endothelial cells co-cultured with SK23. Drosha, miR-9 or miR-183 was knocked down as indicated. * $p < 0.05$, Student's t-test. E. Quantitative PCR of miRNAs in

SK23 MVs treated with RNase in combination with Proteinase K or 0.5% SDS. * $p < 0.05$, Student's t-test. F. Quantitative PCR of miR-9 in SK23 cells, purified MVs or recipient HUVECs co-cultured with MVs. Transfection of anti-miR-9 in SK23 cells resulted in significant decrease of miR-9 expression. * $p < 0.05$, Student's t-test.

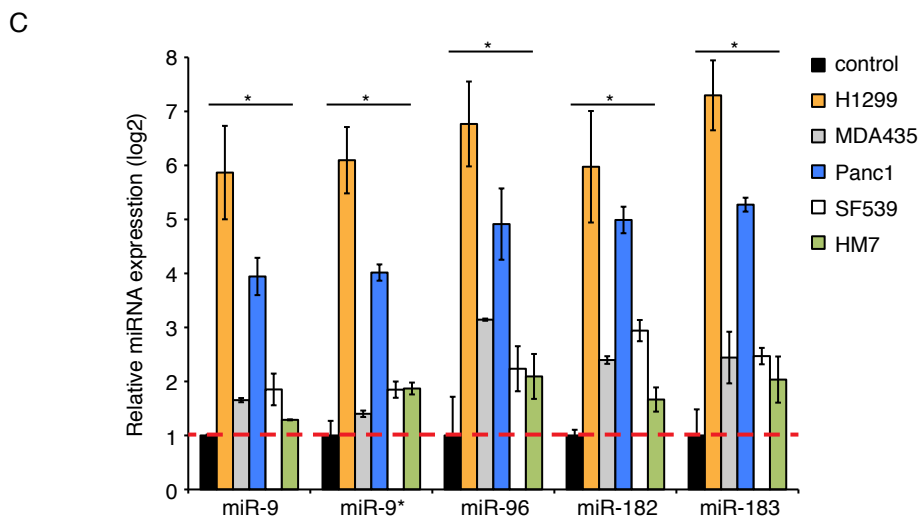
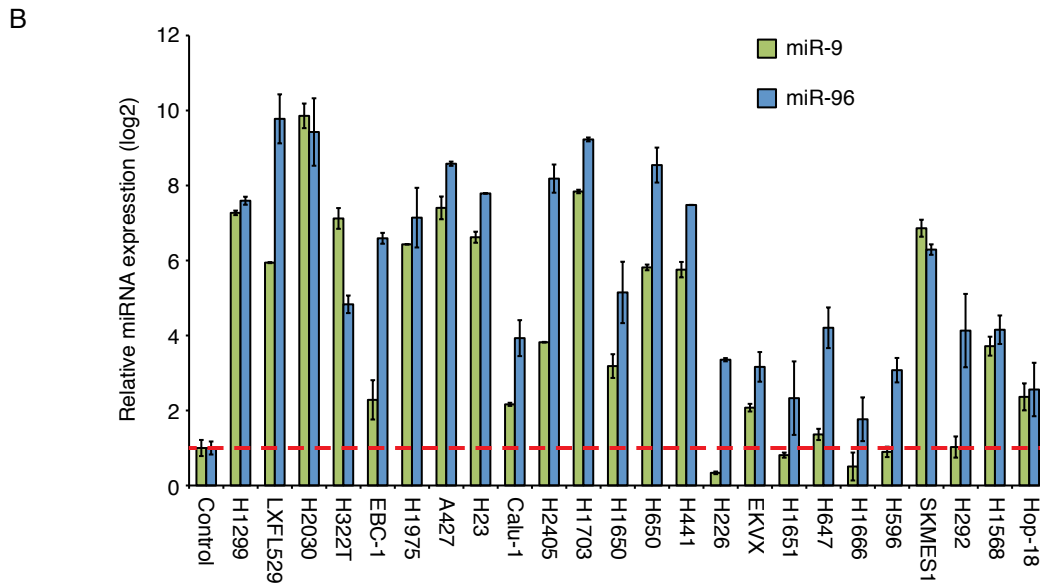
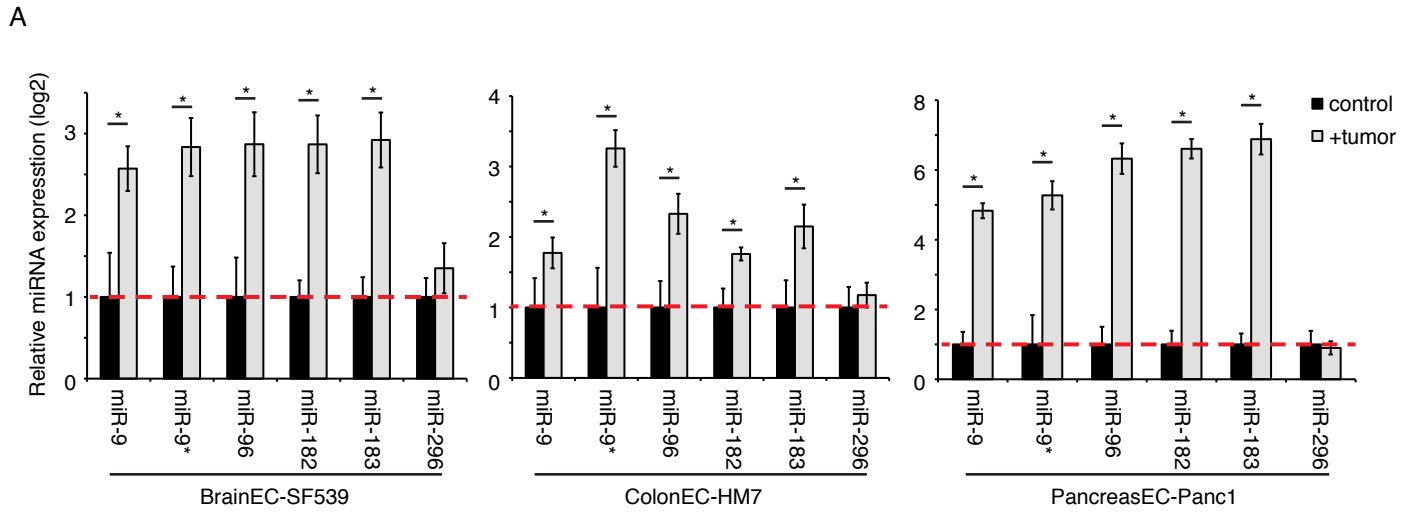
Figure S3. Inhibition of tumor miR-9 decreases endothelial migration without affecting tumor cells. A. Trans-well migration of HUVECs in co-culture with scrambled or anti-miR-9 transfected SK23 cells. B. Effects of anti-miR-9 or siDrosha on tumor cell growth. C. Fifty-five angiogenesis-related proteins in purified SK23 MVs as detected by antibody array.

Figure S4. Anti-miR-9 inhibits angiogenesis and tumor growth in vivo. A. FITC-lectin perfusion assay in HM7 tumor xenografts. B. Quantification of tumor cell proliferation and apoptosis in HM7 tumors treated with scrambled sequence or anti-miR-9.

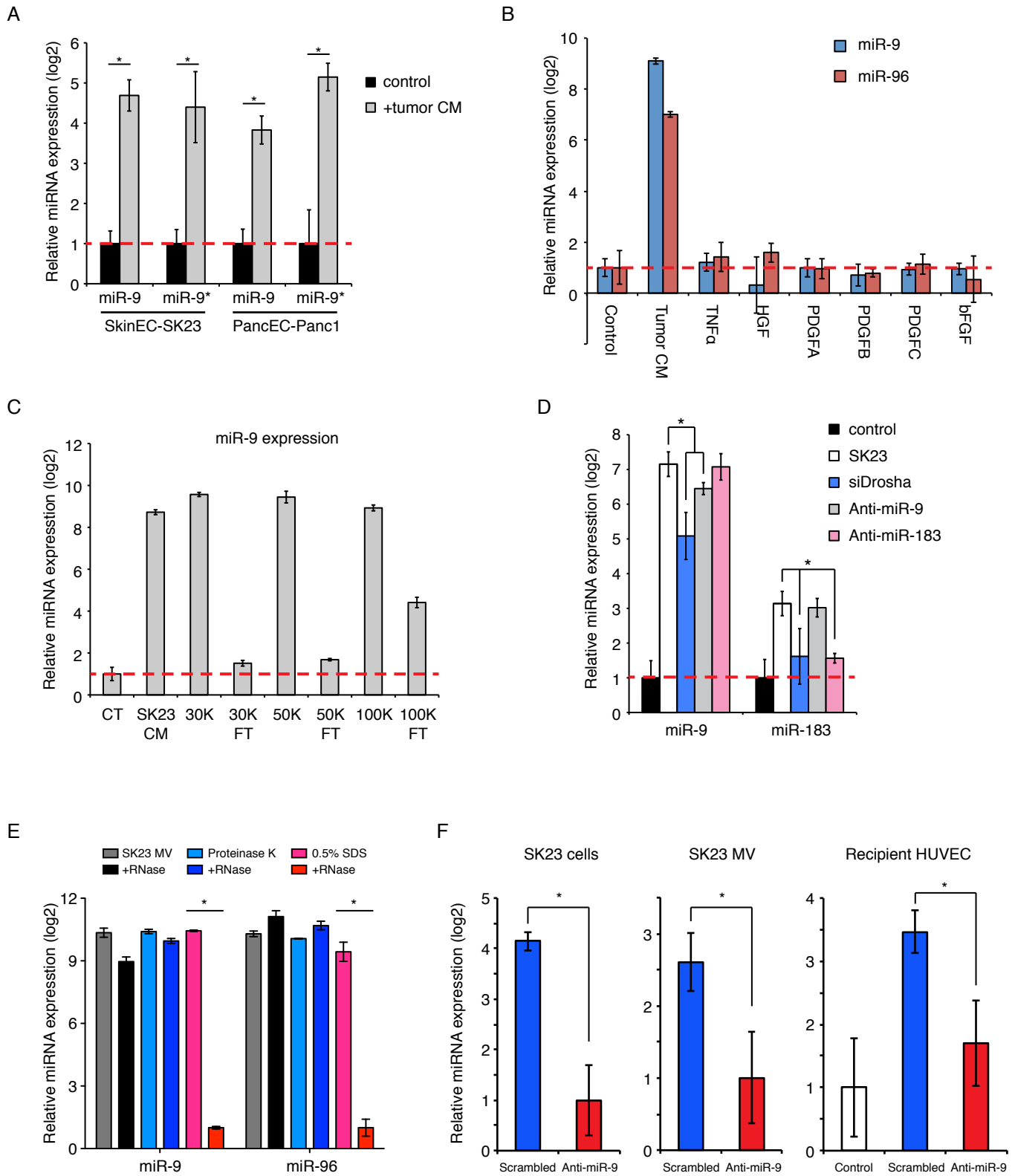
Figure S5. Tumor derived miRNAs activate the JAK-STAT pathway. A. Western blot of HUVECs transfected with individual miRNAs as indicated. B. Endothelial cell proliferation measured by BrdU ELISA. C. Cell

apoptosis in the presence of JAK2 inhibitors revealed by probing PARP and Caspase-3.

Supplementary Figure 1

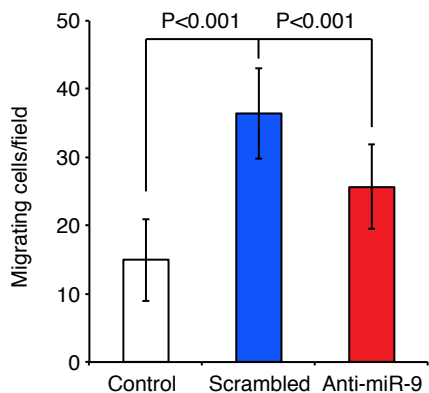


Supplementary Figure 2

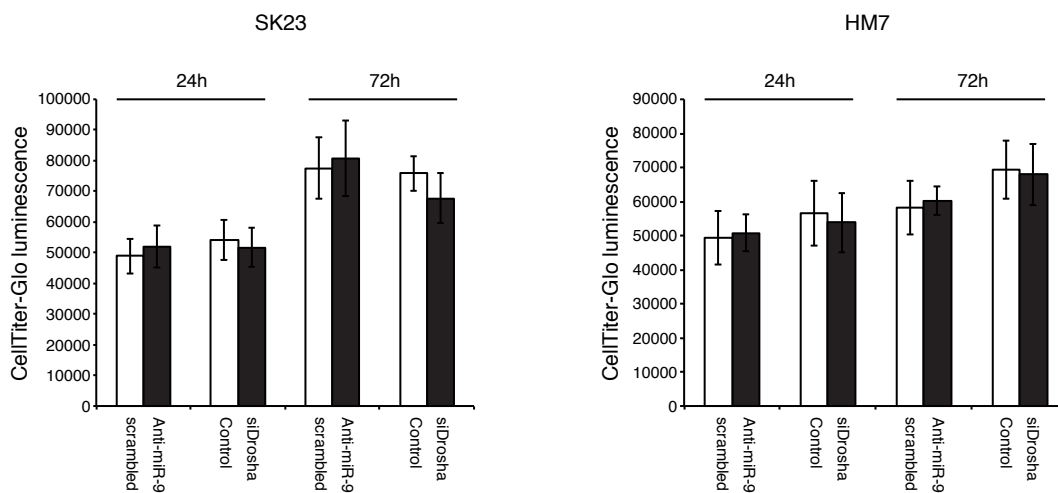


Supplementary Figure 3

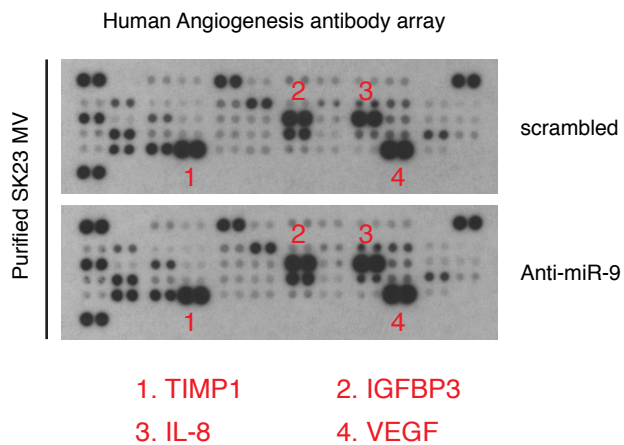
A



B

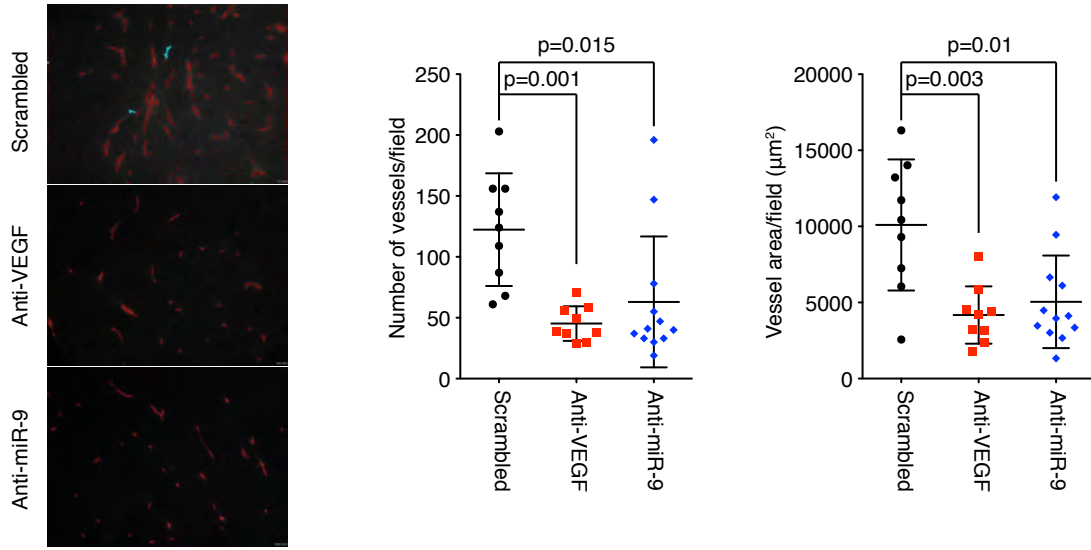


C

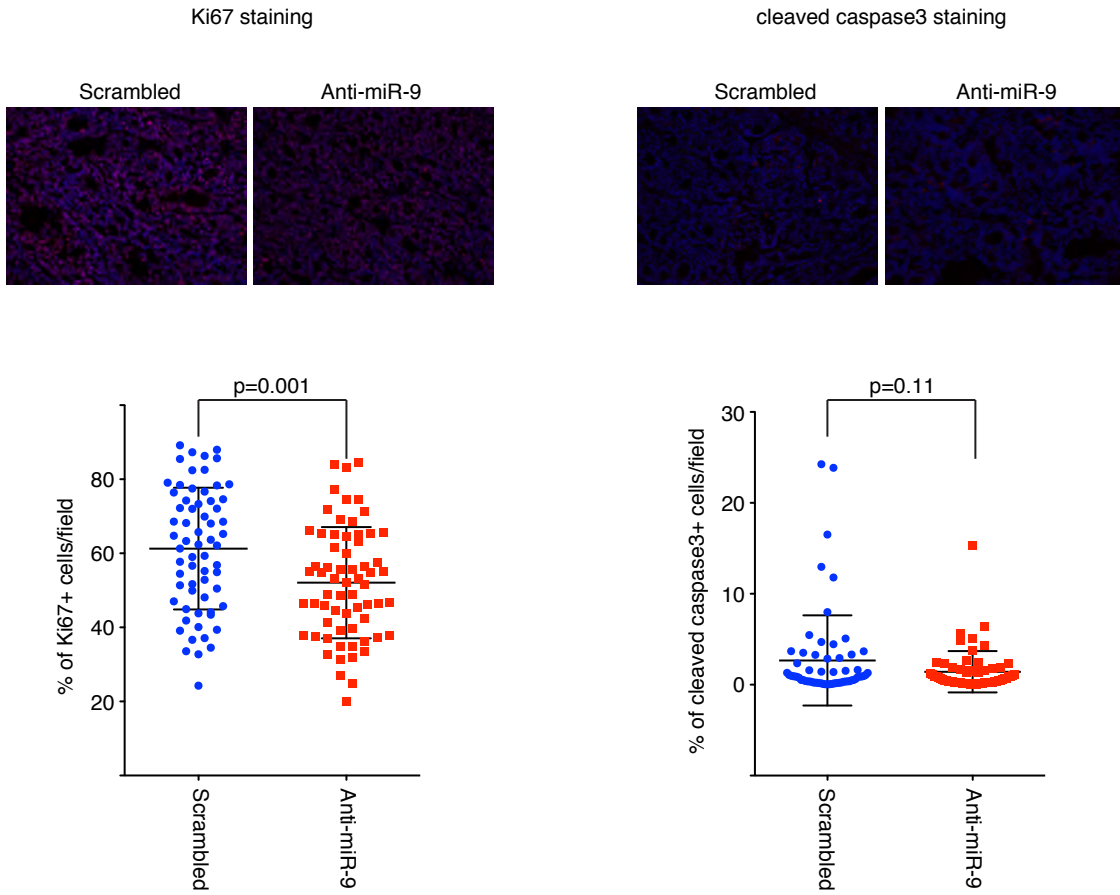


Supplementary Figure 4

A

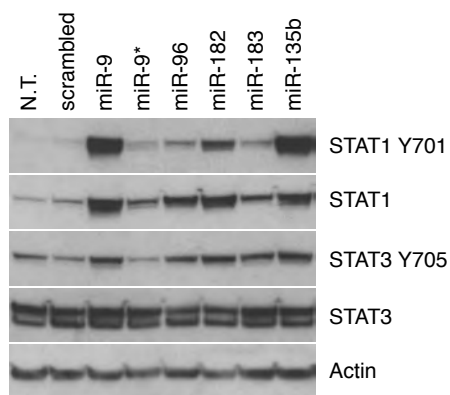


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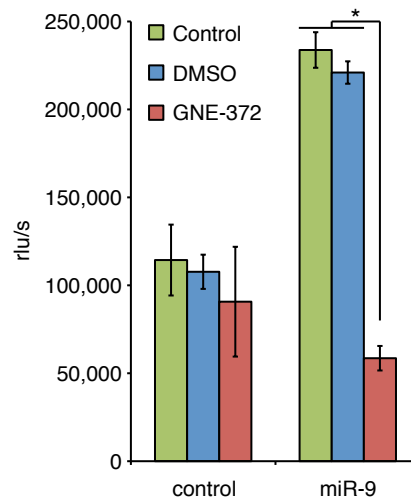


Supplementary Figure 5

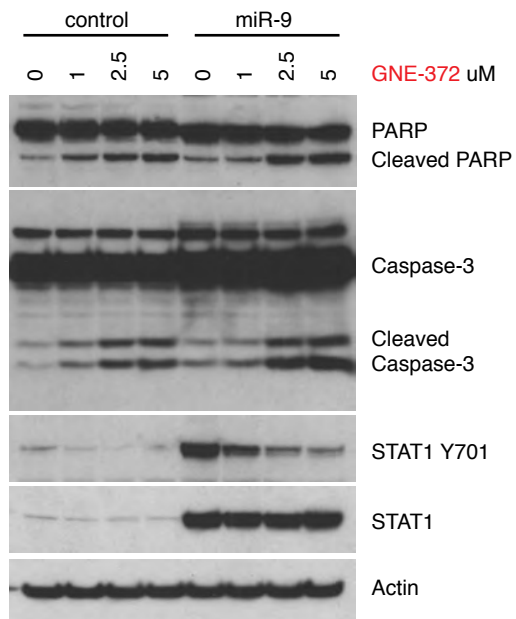
A



B



C



Supplementary Table 1. Differentially expressed miRNAs in endothelial cells in response to tumor cell stimulation.

Lung-H1299		Dermal-MDA435		Pancreas-PANC1		Brain-SF539		Colon-HM7	
miRNA	fold (log2)	miRNA	fold (log2)	miRNA	fold (log2)	miRNA	fold (log2)	miRNA	fold (log2)
hsa-miR-9	5.272	hsa-miR-9	3.023	hsa-miR-9	2.77834375	hsa-miR-9	2.458065037	hsa-miR-9	1.751923562
hsa-miR-10b	2.655	hsa-miR-96	2.1822835	hsa-miR-133a	2.095	hsa-miR-98	-2.207603451	hsa-miR-18b	-1.987416266
hsa-miR-34c-5p	2.334	hsa-miR-182	1.9232835	hsa-miR-135b	4.704	hsa-miR-135b	1.817350391	hsa-miR-95	-1.915581702
hsa-miR-95	1.763	hsa-miR-199a-5p	2.744	hsa-miR-182	2.31534375	hsa-miR-138	1.567920688	hsa-miR-135b	2.470189096
hsa-miR-96	5.1703621	hsa-miR-215	2.9762835	hsa-miR-190	-2.58920112	hsa-miR-139-3p	3.47654343	hsa-miR-139-3p	-2.080485343
hsa-miR-105	3.8833621	hsa-miR-296-5p	1.669	hsa-miR-302c	-1.65920112	hsa-miR-143	7.232872013	hsa-miR-141	3.443840982
hsa-miR-148a	1.624	hsa-miR-363	7.275	hsa-miR-375	-2.204	hsa-miR-145	4.682590488	hsa-miR-148a	-1.74972248
hsa-miR-182	5.2483621	hsa-miR-431	-1.585	hsa-miR-449b	1.899	hsa-miR-223	-2.015958782	hsa-miR-187	-2.047835349
hsa-miR-183	4.8023621	hsa-miR-451	2.386	hsa-miR-616	2.016	hsa-miR-329	-1.760578152	hsa-miR-200a	3.772259713
hsa-miR-187	-2.356382	hsa-miR-504	-1.531	hsa-miR-618	-1.793	hsa-miR-541	-2.088275906	hsa-miR-200b	3.052783014
hsa-miR-190	3.491	hsa-miR-508-3p	4.9512835	hsa-miR-642	2.56	hsa-miR-582-3p	-1.606088635	hsa-miR-200c	2.626645089
hsa-miR-203	7.009	hsa-miR-509-5p	2.5802835	hsa-miR-206	-1.768	hsa-miR-708	-2.183589932	hsa-miR-203	2.357625009
hsa-miR-210	3.469	hsa-miR-642	2.8082835	hsa-miR-380-5p	-2.225	hsa-miR-885-5p	3.337379459	hsa-miR-326	-2.033232688
hsa-miR-296-3p	4.0053621	hsa-miR-651	-1.9747716	hsa-miR-497	-1.757	hsa-miR-659	-2.666884424	hsa-miR-429	3.069556237
hsa-miR-296-5p	5.847	hsa-miR-654-5p	-4.0377716	hsa-miR-500	-1.683	hsa-miR-374a*	-2.081418039	hsa-miR-487a	-1.64428234
hsa-miR-302b	1.8203621	hsa-miR-506	2.1282835	hsa-miR-488	-1.938	hsa-miR-7-2*	1.69789028	hsa-miR-518f	-5.901333808
hsa-miR-449a	3.7063621	hsa-miR-206	-1.826	hsa-miR-516-3p	-2.812	hsa-miR-374b*	-1.530123712	hsa-miR-541	-4.904393195
hsa-miR-449b	4.5563621	hsa-miR-769-3p	-1.7	hsa-miR-564	-5.45972	hsa-miR-1226*	-1.507002832	hsa-miR-206	2.601670264
hsa-miR-451	1.5353621	hsa-miR-9*	2.487	hsa-miR-601	-2.88572	hsa-miR-1269	5.205857276	hsa-miR-622	-1.79489422
hsa-miR-483-5p	2.321	hsa-miR-193b*	1.591	hsa-miR-605	-3.64772	hsa-miR-1255B	1.511204718	hsa-miR-638	4.80663204
hsa-miR-493	1.857	hsa-let-7c*	2.70962875	hsa-miR-638	-1.807	hsa-miR-1183	-1.549248697	hsa-miR-572	1.540444373
hsa-miR-551b	3.4033621	hsa-miR-577	4.10662875	hsa-miR-645	-1.85	hsa-miR-1289	-1.605137445	hsa-miR-580	4.197224615
hsa-miR-642	4.8713621	hsa-miR-1225-3P	-6.41231525	hsa-miR-573	-2.965	hsa-miR-1300	1.773884772	hsa-miR-770-5p	-1.614720346
hsa-miR-885-5p	2.122	hsa-miR-1269	1.77562875	hsa-miR-29c*	-1.512			hsa-miR-939	2.558663367
hsa-miR-30d	1.511	hsa-miR-1183	-4.00631525	hsa-miR-769-3p	-1.628			hsa-miR-26a-1*	-1.555420877
hsa-miR-34b	2.4714285			hsa-miR-221*	-1.525			hsa-miR-191*	-2.05805874
hsa-miR-500	2.9094285			hsa-miR-26a-2*	-1.94			hsa-miR-1305	2.299860953
hsa-miR-592	6.151			hsa-miR-374a*	-1.796			hsa-miR-1275	1.701766013
hsa-miR-641	1.7504285			hsa-miR-377*	-1.86172			hsa-miR-1243	-2.539521219
hsa-miR-572	1.61			hsa-miR-125b-2*	-4.21572			hsa-miR-1248	2.366608618
hsa-miR-34b	1.614			hsa-let-7i*	-1.988				
hsa-miR-93*	1.547			hsa-miR-9*	3.818152				
hsa-miR-100*	2.242			hsa-miR-192*	-2.241				
hsa-miR-27b*	1.532			hsa-miR-30d*	-2.083				
hsa-miR-935	1.717			hsa-let-7a*	-1.54472				
hsa-miR-875-5p	1.898			hsa-miR-744*	-1.695				
hsa-miR-9*	7.636			hsa-miR-125b-1*	-1.581				
hsa-miR-183*	7.5534285			hsa-miR-106b*	-2.108				
hsa-miR-155*	1.862			hsa-let-7c*	-1.736				
hsa-miR-218-2*	-2.123685			hsa-let-7f-1*	-2.81472				
hsa-miR-425*	2.33			hsa-let-7f-2*	-1.794				
hsa-miR-10b*	1.758			hsa-miR-23a*	1.747152				
hsa-miR-483-3p	7.8934285			hsa-miR-338-5P	-2.488				
hsa-miR-125b-1*	2.007			hsa-miR-1225-3P	-7.79272				
hsa-miR-106b*	2.648			hsa-miR-1233	-2.142				
hsa-miR-577	7.3014285			hsa-miR-1179	-2.62272				
hsa-miR-191*	2.786			hsa-miR-1255B	-2.822				
hsa-miR-1226*	3.381			hsa-miR-1282	-2.279				
hsa-miR-1303	4.6444285			hsa-miR-1197	-2.513				
hsa-miR-1183	3.0434285			hsa-miR-1275	-1.587				
hsa-miR-1262	2.17			hsa-miR-1183	-5.23772				
				hsa-miR-1276	-1.927				
				hsa-miR-320B	-1.577				
				hsa-miR-1256	2.101				
				hsa-miR-1262	-3.057				
				hsa-miR-1248	-2.166				