

Supplemental Information

miR-196-5p and miR-107 expression differentiates ocular sebaceous carcinoma from squamous cell carcinoma of the conjunctiva

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Table S1. Differentially expressed microRNAs between squamous cell carcinoma of the conjunctiva (SCCC) and corresponding healthy control tissue. Listed are 79 miRNAs ($p < 0.05$) that are differentially expressed between SCCC ($n=18$) and control tissue (conjunctival squamous epithelium of the eyelid) ($n=6$) and that were used in the supervised hierarchical clustering (Figure 1A). p-values of Mann Whitney U test and false discovery rate p-values (FDR) are listed as well as the average expression level ratios of control/SCCC and SCCC/control.

miRNA	Control/SCCC	SCCC/Control	P-value	FDR
hsa-miR-148a	3.363924	0.297272	0.0001	0.001428
hsa-miR-18b	0.014008	71.38607	0.0001	0.001428
hsa-miR-200c	2.327974	0.429558	0.0001	0.002044
hsa-miR-375	7.901268	0.126562	0.0001	0.002044
hsa-miR-100	2.61338	0.382646	0.0001	0.003746
hsa-miR-139-5p	5.778269	0.173062	0.0001	0.003746
hsa-miR-509-5p	166.6427	0.006001	0.0001	0.004612
hsa-miR-628-5p	2.976465	0.335969	0.0001	0.004612
hsa-miR-328	4.363051	0.229197	0.0001	0.007177
hsa-miR-26b	2.492053	0.401276	0.0001	0.008889
hsa-miR-182	2.729625	0.366351	0.0001	0.010049
hsa-miR-195	2.550753	0.392041	0.0001	0.011027
hsa-miR-146a	4.466717	0.223878	0.0001	0.015449
hsa-miR-508	29.70985	0.033659	0.0001	0.01888
hsa-miR-424	0.029198	34.24947	0.001	0.007177
hsa-miR-574-3p	2.576914	0.388061	0.001	0.008889
hsa-miR-200b	2.302402	0.434329	0.001	0.008889
hsa-miR-18a	0.366928	2.725333	0.001	0.008889
hsa-miR-191	2.515353	0.397559	0.001	0.008965
hsa-miR-99a	2.095678	0.477173	0.001	0.01308
hsa-miR-218	2.675681	0.373737	0.001	0.016045
hsa-miR-126	2.198917	0.454769	0.001	0.017732
hsa-let-7g	2.405634	0.415691	0.001	0.019065
hsa-miR-211	44.39504	0.022525	0.001	0.086494
hsa-let-7c	4.16432	0.240135	0.002	0.007177
hsa-miR-548c-5p	0.069165	14.45814	0.002	0.007653
hsa-miR-139-3p	313.1079	0.003194	0.002	0.014824
hsa-miR-30c	2.109663	0.474009	0.002	0.015463
hsa-miR-26a	2.353042	0.424982	0.002	0.016045
hsa-miR-335	2.273675	0.439817	0.002	0.018827
hsa-miR-29a	2.186995	0.457248	0.002	0.04048
hsa-miR-184	88.17474	0.011341	0.003	0.016045
hsa-miR-183	2.797199	0.3575	0.003	0.023609
hsa-miR-383	30.73477	0.032536	0.003	0.05104
hsa-miR-125a-5p	2.482968	0.402744	0.004	0.016175
hsa-miR-455	0.325801	3.069354	0.004	0.017808
hsa-miR-125b	1.990835	0.502302	0.004	0.021217
hsa-let-7b	2.153847	0.464286	0.004	0.02871

mmu-miR-491	1.731597	0.577502	0.004	0.034014
hsa-miR-186	1.936481	0.516401	0.004	0.037334
hsa-miR-224	0.349602	2.860394	0.004	0.03969
hsa-miR-204	34.29999	0.029155	0.004	0.040969
hsa-miR-423-5p	2.23569	0.447289	0.004	0.054769
hsa-miR-510	23.70807	0.04218	0.005	0.037334
hsa-miR-145	2.20847	0.452802	0.006	0.027343
hsa-miR-21	0.535989	1.865711	0.006	0.034014
hsa-miR-506	28.81457	0.034705	0.006	0.047251
hsa-let-7d	1.748937	0.571776	0.006	0.064436
hsa-miR-22	0.002847	351.2929	0.008	0.008889
mmu-miR-140	1.560827	0.640686	0.008	0.095803
hsa-miR-30b	1.884525	0.530638	0.009	0.03043
hsa-miR-140-3p	2.0204	0.494952	0.009	0.053991
hsa-let-7a	2.526337	0.39583	0.009	0.15602
hsa-miR-708	0.45226	2.211119	0.012	0.081142
hsa-miR-320	2.033516	0.491759	0.015	0.03043
hsa-miR-193a-3p	0.39286	2.545437	0.015	0.075105
hsa-miR-422a	3.133185	0.319164	0.016	0.055552
hsa-let-7^e	1.915082	0.522171	0.016	0.13616
hsa-miR-214	1.907501	0.524246	0.018	0.052541
hsa-miR-532-3p	1.772962	0.564028	0.018	0.064469
hsa-miR-101	2.176836	0.459382	0.0185	0.053991
hsa-miR-130b	0.476517	2.09856	0.02	0.064469
hsa-miR-579	0.055099	18.14913	0.022	0.040969
hsa-miR-345	1.778152	0.562382	0.022	0.06593
hsa-miR-548d-5p	0.123125	8.121818	0.022	0.06593
hsa-miR-429	1.933766	0.517126	0.022	0.137874
hsa-miR-185	0.615875	1.623707	0.027	0.074389
hsa-miR-23b	33.44478	0.0299	0.027	0.218984
hsa-miR-891a	10.50865	0.09516	0.029	0.054769
hsa-miR-338-3p	4.614451	0.216711	0.03	0.265803
hsa-miR-484	1.471226	0.679705	0.033	0.125358
hsa-miR-138	2.2001	0.454525	0.033	0.181722
hsa-miR-200a	1.758164	0.568775	0.037	0.246984
hsa-miR-222	2.157112	0.463583	0.04	0.13616
mmu-miR-187	0.291636	3.42893	0.046	0.405157
hsa-miR-331-5p	0.05677	17.6149	0.047	0.064469
hsa-miR-671-3p	1.532939	0.652342	0.047	0.105328
hsa-miR-885-5p	3.546121	0.281998	0.047	0.115283
hsa-miR-518d	7.561453	0.13225	0.048	0.239144

Table S2. Differentially expressed microRNAs between ocular sebaceous carcinoma (OSC) and corresponding healthy control tissue. Listed are 78 miRNAs ($p < 0.05$) that are differentially expressed between OSC ($n=14$) and control tissue (Meibomian glands) ($n=6$) and that were used in the supervised hierarchical clustering (Figure 1B). p -values of Mann Whitney U test and false discovery rate p -values (FDR) are listed as well as the average expression level ratios of control/OSC and OSC/control.

miRNA	Control/OSC	OSC/Control	P-value	FDR
hsa-miR-139-5p	3.726178	0.268371	0.0001	0.000301465
hsa-miR-199a-3p	2.496246	0.400602	0.0001	0.000301465
hsa-miR-328	2.918013	0.342699	0.0001	0.000301465
hsa-miR-130b	0.401121	2.493013	0.0001	0.000301465
hsa-miR-376c	3.114404	0.321089	0.0001	0.000301465
hsa-miR-31	0.139595	7.163568	0.001	0.000301465
hsa-miR-383	75.38322	0.013266	0.001	0.000301465
hsa-miR-139-3p	106.1066	0.009424	0.001	0.000301465
hsa-miR-15a	0.010381	96.32702	0.001	0.000301465
hsa-miR-204	13.83021	0.072305	0.001	0.000301465
hsa-miR-487b	3.040194	0.328926	0.001	0.000301465
hsa-miR-125b	2.044631	0.489086	0.002	0.000301465
hsa-miR-21	0.351752	2.842911	0.002	0.000301465
hsa-miR-494	0.297415	3.362309	0.002	0.000301465
hsa-miR-574-3p	2.222661	0.449911	0.002	0.000301465
hsa-miR-193a-5p	2.750874	0.363521	0.002	0.000301465
hsa-miR-335	2.730895	0.36618	0.002	0.000301465
hsa-miR-296	3.84469	0.260099	0.002	0.000301465
hsa-miR-182	2.259389	0.442598	0.002	0.000301465
hsa-miR-100	2.336035	0.428076	0.003	0.000301465
hsa-miR-886-5p	0.318795	3.136816	0.003	0.000301465
hsa-miR-338-3p	4.648259	0.215134	0.003	0.000301465
hsa-miR-874	106.1133	0.009424	0.005	0.000301465
hsa-miR-504	89.59001	0.011162	0.005	0.005102499
hsa-miR-214	1.954108	0.511743	0.005	0.02594702
hsa-miR-127	2.028345	0.493013	0.005	0.02594702
mmu-miR-187	0.057611	17.35784	0.005	0.02594702
hsa-miR-195	1.901813	0.525814	0.005	0.02594702
hsa-miR-520b	0.075829	13.18763	0.006	0.02594702
hsa-miR-125a-5p	2.036363	0.491072	0.006	0.062187074
hsa-miR-500	0.502096	1.991649	0.006	0.071335425
hsa-miR-636	0.255577	3.912718	0.007	0.074872408
hsa-miR-106b	0.350331	2.854446	0.009	0.074872408
hsa-miR-655	4.508368	0.22181	0.009	0.074872408
hsa-miR-422a	3.84747	0.259911	0.009	0.074872408
hsa-miR-485-3p	4.506542	0.2219	0.009	0.074872408
hsa-miR-503	0.128631	7.774191	0.01	0.074872408
hsa-miR-212	0.499498	2.002009	0.012	0.074872408
hsa-miR-329	5.324067	0.187826	0.012	0.100211609
hsa-miR-660	0.534102	1.872301	0.012	0.100211609
hsa-miR-155	0.285607	3.501309	0.012	0.100211609
hsa-miR-135b	0.141648	7.059741	0.012	0.100211609
hsa-miR-185	0.558834	1.789439	0.015	0.100211609
hsa-miR-140-3p	2.73765	0.365277	0.015	0.100211609
hsa-miR-542-3p	0.113813	8.786305	0.015	0.100211609
hsa-miR-449	0.114493	8.734165	0.015	0.100211609
hsa-miR-148a	1.602759	0.623924	0.015	0.100211609
hsa-miR-196b	0.058826	16.99936	0.02	0.100211609

hsa-miR-126	1.850234	0.540472	0.02	0.109573987
hsa-miR-483-5p	0.516552	1.935915	0.02	0.109573987
hsa-miR-365	2.564304	0.389969	0.02	0.109573987
hsa-miR-193b	2.117824	0.472183	0.02	0.109573987
mmu-miR-495	2.656914	0.376376	0.02	0.109573987
hsa-miR-133b	16.64768	0.060068	0.022	0.109573987
hsa-miR-542-5p	0.073944	13.52377	0.023	0.109573987
hsa-miR-9	0.131343	7.613652	0.026	0.143452639
hsa-miR-28	0.575362	1.738035	0.026	0.145555496
hsa-miR-345	0.467307	2.139922	0.026	0.145555496
hsa-miR-548c-5p	0.106316	9.405941	0.029	0.145555496
hsa-miR-331-5p	0.045249	22.09972	0.03	0.153083206
hsa-let-7f	3.506015	0.285224	0.032	0.163268208
hsa-miR-517a	3.037029	0.329269	0.033	0.163268208
hsa-miR-99a	1.978096	0.505537	0.033	0.163268208
hsa-miR-133a	7.441203	0.134387	0.033	0.163268208
hsa-miR-744	0.595053	1.680523	0.033	0.163268208
hsa-miR-218	1.544023	0.647659	0.033	0.163268208
hsa-miR-517c	2.756074	0.362835	0.033	0.163268208
hsa-miR-145	1.65455	0.604394	0.033	0.163268208
hsa-miR-135a	0.318652	3.138217	0.034	0.163268208
mmu-miR-451	0.348596	2.868649	0.036	0.163268208
mmu-miR-93	0.436937	2.288659	0.036	0.163268208
hsa-miR-23b	41.3399	0.02419	0.037	0.163268208
hsa-miR-99b	1.489505	0.671364	0.041	0.163268208
hsa-miR-512-3p	2.623971	0.381102	0.041	0.163268208
hsa-miR-411	1.494263	0.669226	0.044	0.163268208
hsa-miR-525-3p	10.71605	0.093318	0.046	0.163268208
hsa-miR-548d-5p	0.169179	5.910906	0.046	0.183454131
hsa-let-7c	1.861897	0.537087	0.046	0.183454131

Table S3. Differentially expressed microRNAs between primary squamous cell carcinoma of the conjunctiva that metastasize (SCCC_m) and those that do not (SCCC-). Listed are 16 miRNAs (p<0.05) that are differentially expressed between primary SCCC (n=18) that eventually display metastases (SCCC_m) and those that did not metastasize in the time-frame of the follow-up (SCCC-) and that were used in the supervised hierarchical clustering (Figure 2A). p-values of Mann Whitney U test and false discovery rate p-values (FDR) are listed as well as the average expression level ratios of SCCC-/SCCC_m and SCCC_m/SCCC-

miRNA	SCCC-/SCCC _m	SCCC _m /SCCC-	P- value	FDR
hsa-miR-409-5p	0.087115	11.47902	0.002	0.468
hsa-miR-590-5p	1.879544	0.532044	0.004	0.468
hsa-miR-198	0.375235	2.664998	0.007	0.468
hsa-miR-32	5.346134	0.187051	0.007	0.5482
hsa-miR-143	0.612528	1.632578	0.008	0.5482
hsa-miR-629	0.129307	7.733511	0.008	0.5482
hsa-miR-548c	0.102292	9.775917	0.015	0.468
hsa-miR-99b	0.61549	1.624722	0.015	0.5157
hsa-miR-125b	0.60897	1.642116	0.027	0.5482
hsa-miR-199a	0.179127	5.582624	0.029	0.669
hsa-miR-505	0.104684	9.552585	0.031	0.669
hsa-miR-362	0.636025	1.572266	0.035	0.5482
hsa-miR-345	0.648909	1.541048	0.044	0.669
hsa-miR-34a	0.667004	1.499241	0.044	0.669
hsa-miR-335	1.617858	0.618101	0.048	0.669

Table S4. Differentially expressed microRNAs between ocular sebaceous carcinoma that recur (OSC_R) and those that do not recur (OSC-). Listed are 8 miRNAs (p<0.05) that are differentially expressed between primary OSC (n=14) that eventually recur (OSC_R) and those that did not recur in the time-frame of the follow-up (OSC-) and that were used in the supervised hierarchical clustering (Figure 2B). p-values of Mann Whitney U test and false discovery rate p-values (FDR) are listed as well as the average expression level ratios of OSC-/OSC_R and OSC_R/OSC-.

miRNA	OSC-/OSC _R	OSC _R /OSC-	P-value	FDR
hsa-miR-525-3p	7,556668	0,132333	0,022	0,901513
hsa-miR-219-1-3p	21,36382	0,046808	0,032	0,901513
hsa-miR-517b	5,566092	0,179659	0,043	0,901513
hsa-miR-888	6,980908	0,143248	0,043	0,901513
hsa-miR-506	12,20891	0,081907	0,043	0,901513
hsa-miR-508	13,01921	0,07681	0,043	0,901513
hsa-miR-411	0,551286	1,81394	0,043	0,901513
hsa-miR-487b	0,336554	2,971289	0,043	0,901513

Table S5. Differentially expressed microRNAs between squamous cell carcinoma of the conjunctiva (SCCC) and ocular sebaceous carcinoma (OSC). Listed are 38 miRNAs ($p < 0.05$) that are differentially expressed between SCCC ($n=18$) and OSC ($n=14$) and that were used in the supervised hierarchical clustering (Figure 3). p -values of Mann Whitney U test and false discovery rate p -values (FDR) are listed as well as the average expression level ratios of control/SCCC and SCCC/control.

miRNA	OSC/SCCC	SCCC/OSC	P-value	FDR
hsa-miR-152	0.549082	1.821222	0.0001	0.05408456
hsa-miR-885-5p	6.304642	0.158613	0.001	0.05408456
hsa-miR-191	2.647099	0.377772	0.001	0.055200656
hsa-miR-223	0.357044	2.800774	0.001	0.055200656
mmu-miR-124a	0.1435	6.968617	0.001	0.153161901
hsa-miR-455	0.333646	2.997191	0.002	0.055200656
hsa-miR-183	3.464555	0.288637	0.002	0.056371921
hsa-miR-107	17.86865	0.055964	0.002	0.101364558
hsa-miR-375	4.561179	0.219242	0.004	0.100487348
hsa-miR-9	7.334788	0.136337	0.005	0.071816105
hsa-miR-455-3p	0.411753	2.428641	0.005	0.153161901
hsa-miR-425-5p	2.421695	0.412934	0.007	0.133361292
hsa-miR-196b	0.152276	6.567035	0.007	0.135762401
hsa-miR-493-3p	0.314701	3.177615	0.009	0.357218414
hsa-miR-494	0.448891	2.227713	0.014	0.135762401
hsa-miR-138	0.463725	2.156453	0.014	0.294185387
hsa-miR-21	0.599696	1.667511	0.016	0.144977075
hsa-miR-30c	1.847739	0.541202	0.017	0.176456266
hsa-miR-101	2.070469	0.482982	0.018	0.118185238
hsa-miR-148b	2.851371	0.350708	0.02	0.231117144
hsa-miR-182	2.034129	0.491611	0.02	0.283798459
hsa-miR-99b	0.712166	1.404166	0.02	0.29024011
hsa-miR-590-5p	1.703094	0.587167	0.022	0.283798459
hsa-miR-655	0.387705	2.579283	0.022	0.379726354
hsa-miR-32	2.279261	0.438739	0.023	0.560289283
hsa-miR-135b	0.241916	4.133674	0.024	0.29024011
hsa-miR-642	0.510223	1.959926	0.025	0.439894732
hsa-miR-449	3.217069	0.310842	0.026	0.446197609
hsa-miR-532-3p	1.386819	0.721075	0.027	0.357218414
hsa-miR-509-5p	7.775498	0.128609	0.031	0.357218414
hsa-miR-490	0.089071	11.22701	0.033	0.105338384
mmu-miR-491	1.478838	0.676206	0.034	0.276178304
hsa-miR-376c	0.470283	2.126379	0.034	0.456599223
hsa-miR-483-5p	0.592341	1.688216	0.037	0.357218414
hsa-miR-891a	4.350374	0.229865	0.041	0.357218414
hsa-let-7g	1.605626	0.62281	0.047	0.379726354
hsa-miR-127	0.626917	1.595108	0.049	0.343479638
hsa-miR-454	0.723781	1.381634	0.049	0.535630419

Figure S1

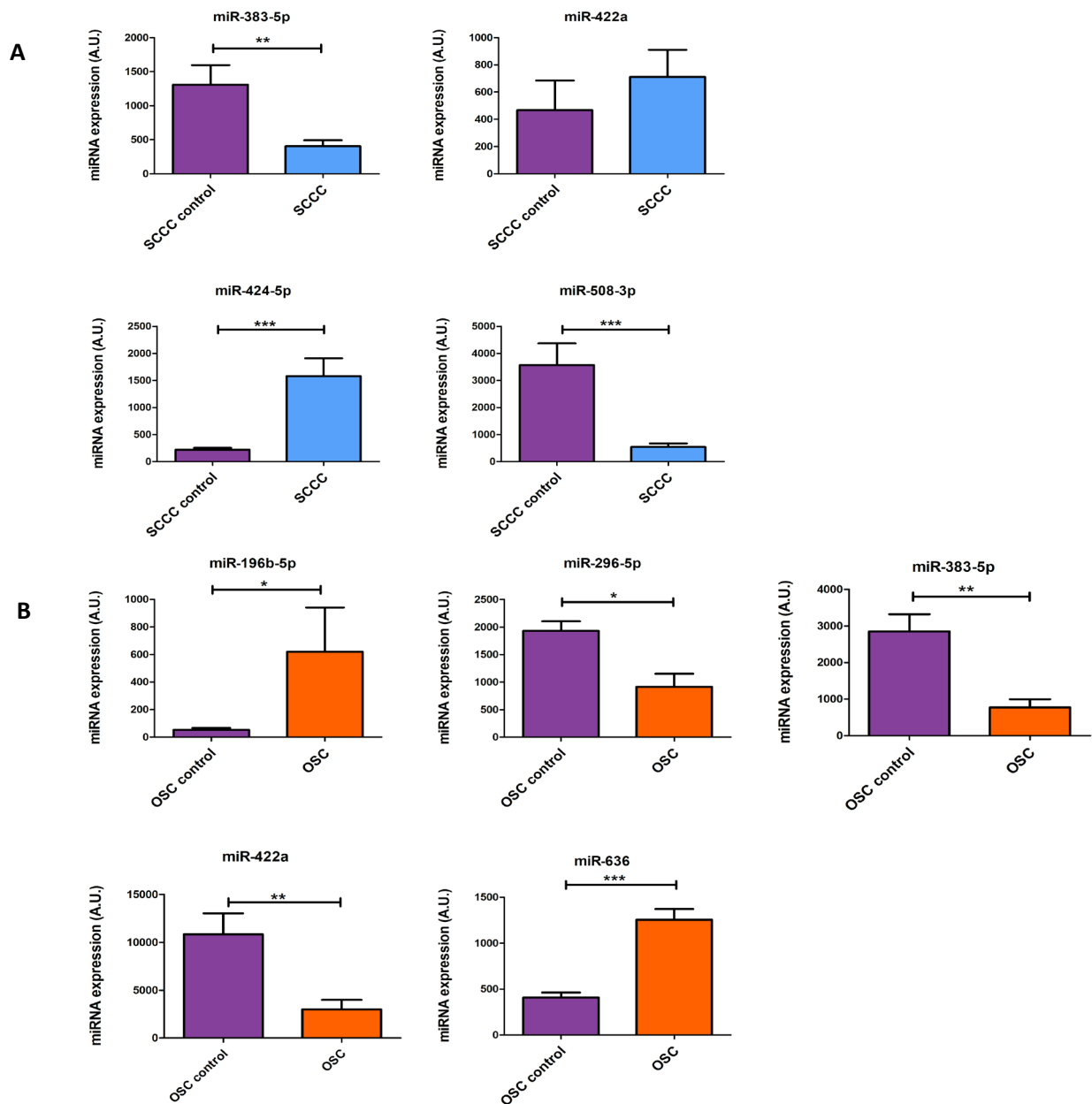


Figure S1. Quantitative RT-PCR verification of selected differentially expressed microRNAs in squamous cell carcinoma of the conjunctiva (SCCC) and ocular sebaceous carcinoma (OSC) and their corresponding control tissues. (A) A standardized RT-PCR procedure using individual assays was used to verify the expression of selected miRNAs found differentially expressed between SCCC and healthy control tissue (conjunctival squamous epithelium of the eyelid). The expression of miR-383-5p, miR-422a, miR-424-5p and miR-508-3p was determined in the original discovery cohort consisting of 18 SCCC and 6 control samples. (B) A standardized RT-PCR procedure using individual assays was used to verify the expression of selected miRNAs found differentially expressed between OSC and healthy control tissue (Meibomian glands). The expression of miR-196b-5p, miR-296-5p, miR-383-5p, miR-422a and miR-636 was determined in the original discovery cohort consisting of 14 OSC and 6 control samples. A standard dilution series of a cDNA samples-pool was used to determine absolute quantification of the miRNA expression. Depicted are average values \pm S.D. Asterisks indicate statistically significant differences * $p < 0.05$; ** $p < 0.005$ and *** $p < 0.0005$ (Mann Whitney U test)

Figure S2

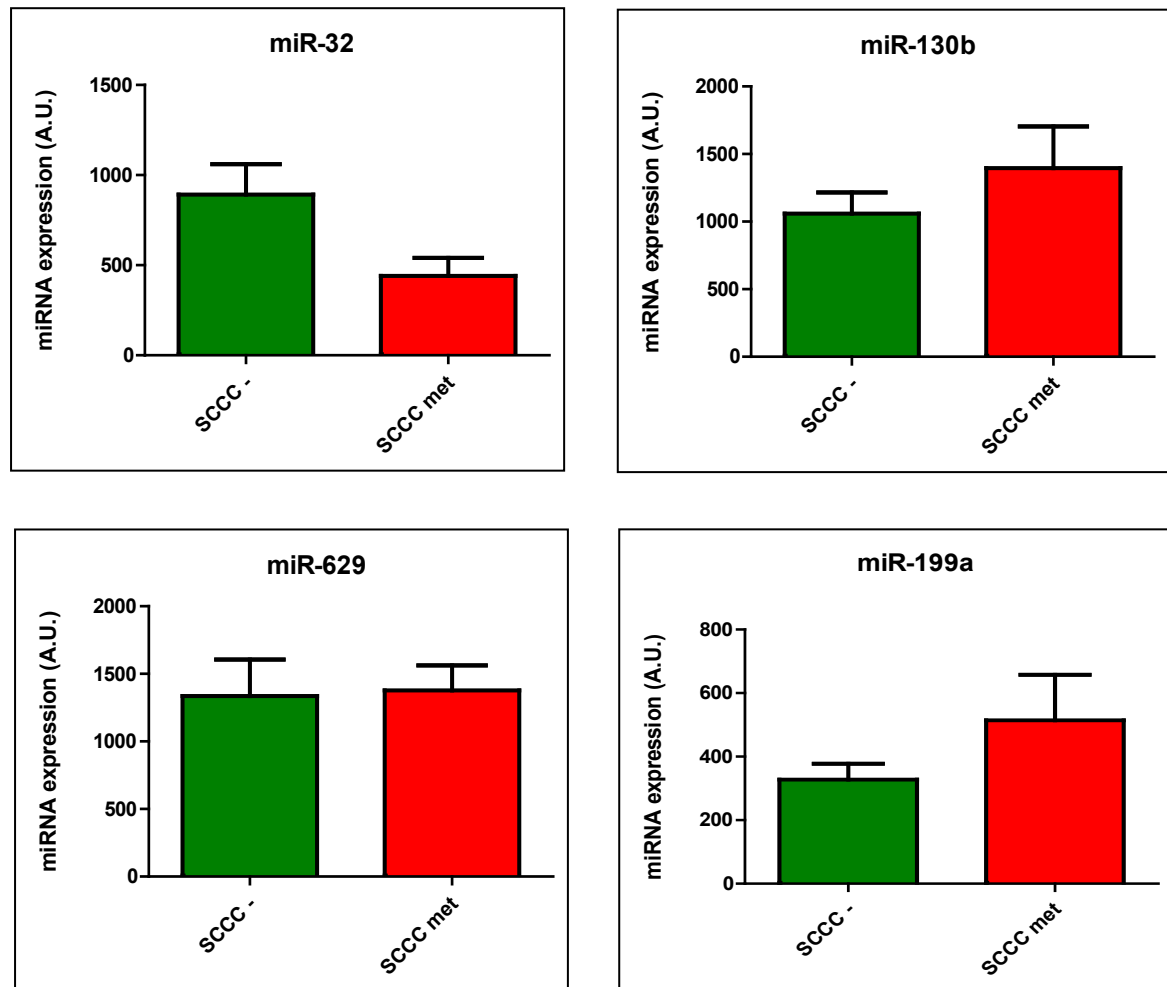
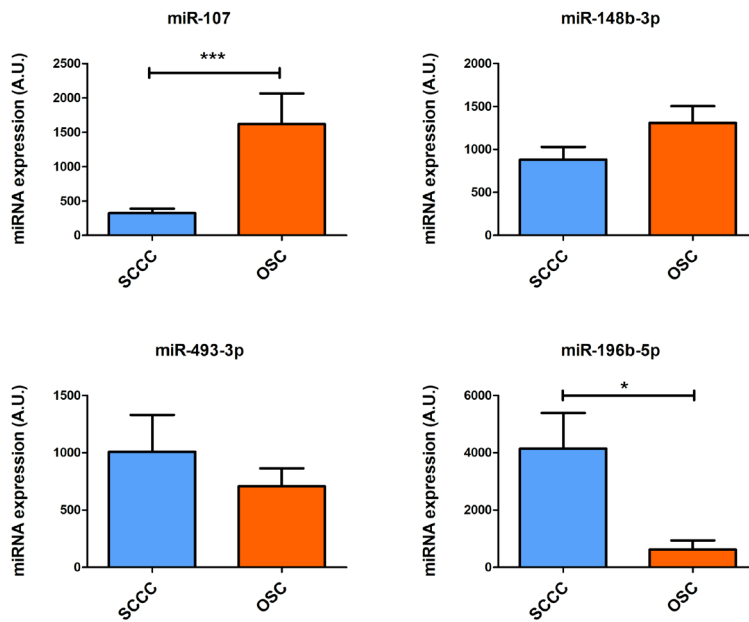


Figure S2. Quantitative RT-PCR verification of selected differentially expressed microRNAs in squamous cell carcinoma of the conjunctiva that metastasize (SCCC_{met}) and those that do not (SCCC₋). A standardized RT-PCR procedure using individual assays was used to verify the expression of selected miRNAs found differentially expressed between primary SCCC (n=18) that eventually display metastases (SCCC_{met}) and those that did not metastasize in the time-frame of the follow-up (SCCC₋) and that were used in the supervised hierarchical clustering (Figure 2A).

Figure S3

A



B

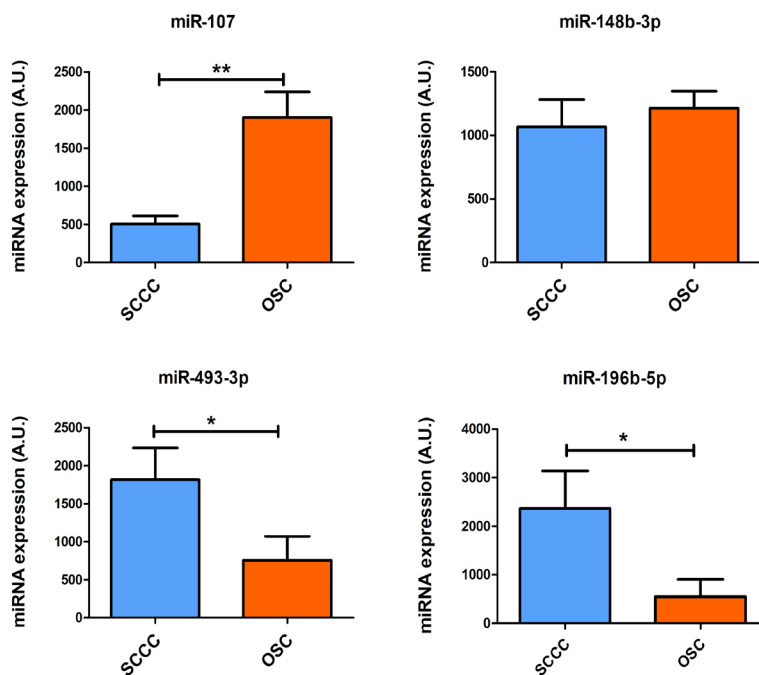


Figure S3. Quantitative RT-PCR verification of selected differentially expressed microRNAs in squamous cell carcinoma of the conjunctiva (SCCC) and ocular sebaceous carcinoma (OSC). A standardized RT-PCR procedure using individual assays was used to verify the expression of selected miRNAs found differentially expressed between SCCC and OSC (see Figure 3). The expression of miR-107, miR-148-3p, miR-196b-5p and miR-493-3p was determined in (A) the original discovery cohort consisting of 18 SCCC and 14 OSC samples and (B) an independent validation cohort consisting of 12 SCCC and 11 OSC samples. A standard dilution series of a cDNA samples-pool was used to determine absolute quantification of the miRNA expression. Depicted are average values \pm S.D. Asterisks indicate statistically significant differences * p<0.05; ** p<0.005 and *** p<0.0005 (Mann Whitney U test).

Figure S4

Sublist	Category	Term	RT	Genes	Count	%	P-Value	Benjamini
<input type="checkbox"/>	KEGG_PATHWAY	MAPK signaling pathway	RT		53	3.0	2.2E-6	7.3E-4
<input type="checkbox"/>	KEGG_PATHWAY	Proteoglycans in cancer	RT		37	2.1	9.6E-5	1.6E-2
<input type="checkbox"/>	KEGG_PATHWAY	Endocytosis	RT		42	2.4	1.7E-4	1.7E-2
<input type="checkbox"/>	KEGG_PATHWAY	Relaxin signaling pathway	RT		26	1.5	2.3E-4	1.7E-2
<input type="checkbox"/>	KEGG_PATHWAY	Ras signaling pathway	RT		39	2.2	2.8E-4	1.7E-2
<input type="checkbox"/>	KEGG_PATHWAY	Oxytocin signaling pathway	RT		29	1.6	3.1E-4	1.7E-2
<input type="checkbox"/>	KEGG_PATHWAY	Colorectal cancer	RT		19	1.1	6.6E-4	3.1E-2
<input type="checkbox"/>	KEGG_PATHWAY	Signaling pathways regulating pluripotency of stem cells	RT		26	1.5	1.2E-3	3.5E-2
<input type="checkbox"/>	KEGG_PATHWAY	Adipocytokine signaling pathway	RT		16	0.9	1.2E-3	3.5E-2
<input type="checkbox"/>	KEGG_PATHWAY	Chronic myeloid leukemia	RT		17	1.0	1.2E-3	3.5E-2
<input type="checkbox"/>	KEGG_PATHWAY	Human cytomegalovirus infection	RT		36	2.0	1.2E-3	3.5E-2
<input type="checkbox"/>	KEGG_PATHWAY	Focal adhesion	RT		33	1.9	1.3E-3	3.5E-2
<input type="checkbox"/>	KEGG_PATHWAY	Yersinia infection	RT		25	1.4	1.4E-3	3.5E-2
<input type="checkbox"/>	KEGG_PATHWAY	Pathways in cancer	RT		69	3.9	2.5E-3	5.7E-2
<input type="checkbox"/>	KEGG_PATHWAY	Rap1 signaling pathway	RT		33	1.9	2.8E-3	5.7E-2
<input type="checkbox"/>	KEGG_PATHWAY	Prostate cancer	RT		19	1.1	2.8E-3	5.7E-2
<input type="checkbox"/>	KEGG_PATHWAY	Kaposi sarcoma-associated herpesvirus infection	RT		31	1.8	3.0E-3	5.7E-2
<input type="checkbox"/>	KEGG_PATHWAY	Viral carcinogenesis	RT		32	1.8	3.3E-3	5.8E-2
<input type="checkbox"/>	KEGG_PATHWAY	FoxO signaling pathway	RT		23	1.3	3.7E-3	5.8E-2
<input type="checkbox"/>	KEGG_PATHWAY	Prolactin signaling pathway	RT		15	0.9	4.0E-3	5.8E-2
<input type="checkbox"/>	KEGG_PATHWAY	ErbB signaling pathway	RT		17	1.0	4.1E-3	5.8E-2
<input type="checkbox"/>	KEGG_PATHWAY	Dopaminergic synapse	RT		23	1.3	4.1E-3	5.8E-2
<input type="checkbox"/>	KEGG_PATHWAY	Hedgehog signaling pathway	RT		13	0.7	4.1E-3	5.8E-2
<input type="checkbox"/>	KEGG_PATHWAY	Human papillomavirus infection	RT		46	2.6	4.4E-3	5.8E-2
<input type="checkbox"/>	KEGG_PATHWAY	Autophagy - animal	RT		24	1.4	4.5E-3	5.8E-2
<input type="checkbox"/>	KEGG_PATHWAY	Melanoma	RT		15	0.9	5.2E-3	6.4E-2
<input type="checkbox"/>	KEGG_PATHWAY	Neurotrophin signaling pathway	RT		21	1.2	5.5E-3	6.4E-2
<input type="checkbox"/>	KEGG_PATHWAY	Growth hormone synthesis, secretion and action	RT		21	1.2	5.5E-3	6.4E-2
<input type="checkbox"/>	KEGG_PATHWAY	Insulin signaling pathway	RT		23	1.3	6.5E-3	7.3E-2
<input type="checkbox"/>	KEGG_PATHWAY	Endocrine resistance	RT		18	1.0	7.3E-3	7.9E-2
<input type="checkbox"/>	KEGG_PATHWAY	Glioma	RT		15	0.9	7.5E-3	7.9E-2
<input type="checkbox"/>	KEGG_PATHWAY	Adherens junction	RT		14	0.8	1.1E-2	1.2E-1
<input type="checkbox"/>	KEGG_PATHWAY	Osteoclast differentiation	RT		21	1.2	1.2E-2	1.2E-1
<input type="checkbox"/>	KEGG_PATHWAY	AMPK signaling pathway	RT		20	1.1	1.3E-2	1.2E-1
<input type="checkbox"/>	KEGG_PATHWAY	T cell receptor signaling pathway	RT		18	1.0	1.3E-2	1.2E-1
<input type="checkbox"/>	KEGG_PATHWAY	Estrogen signaling pathway	RT		22	1.3	1.4E-2	1.3E-1
<input type="checkbox"/>	KEGG_PATHWAY	Platelet activation	RT		20	1.1	1.8E-2	1.5E-1
<input type="checkbox"/>	KEGG_PATHWAY	Wnt signaling pathway	RT		25	1.4	1.8E-2	1.5E-1
<input type="checkbox"/>	KEGG_PATHWAY	Adrenergic signaling in cardiomyocytes	RT		23	1.3	1.8E-2	1.5E-1
<input type="checkbox"/>	KEGG_PATHWAY	Salmonella infection	RT		34	1.9	1.9E-2	1.6E-1
<input type="checkbox"/>	KEGG_PATHWAY	Pancreatic cancer	RT		14	0.8	2.0E-2	1.6E-1
<input type="checkbox"/>	KEGG_PATHWAY	Tight junction	RT		25	1.4	2.0E-2	1.6E-1
<input type="checkbox"/>	KEGG_PATHWAY	Melanogenesis	RT		17	1.0	2.1E-2	1.6E-1
<input type="checkbox"/>	KEGG_PATHWAY	PI3K-Akt signaling pathway	RT		45	2.6	2.2E-2	1.7E-1
<input type="checkbox"/>	KEGG_PATHWAY	Schizophrenia signaling pathway	RT		19	1.1	2.3E-2	1.7E-1
<input type="checkbox"/>	KEGG_PATHWAY	TGF-beta signaling pathway	RT		16	0.9	2.3E-2	1.7E-1
<input type="checkbox"/>	KEGG_PATHWAY	Longevity regulating pathway - multiple species	RT		12	0.7	2.4E-2	1.7E-1
<input type="checkbox"/>	KEGG_PATHWAY	Toxoplasmosis	RT		18	1.0	2.6E-2	1.7E-1
<input type="checkbox"/>	KEGG_PATHWAY	EGFR tyrosine kinase inhibitor resistance	RT		14	0.8	2.7E-2	1.7E-1
<input type="checkbox"/>	KEGG_PATHWAY	Breast cancer	RT		22	1.3	2.7E-2	1.7E-1

Figure S4. KEGG pathway analysis using predicted gene targets of deregulated microRNAs in OSC. The predicted gene targets of miR-196b-5p, miR-296-5p, miR-383-5p, miR-422a and miR-636, all deregulated in OSC versus healthy control tissue, were downloaded from TargetScan (release 8.0; <https://www.targetscan.org>). The genes were subsequently used as input for the database for annotation, visualization and integrated discovery (DAVID- 2021 update; <https://david.ncifcrf.gov>) for a KEGG pathways analysis. Listed are the top 50 most significant pathways.

Figure S5

Sublist	Category	Term	RT	Genes	Count	%	P-Value	Benjamini
<input type="checkbox"/>	KEGG_PATHWAY	Breast cancer	RT		36	1.8	5.0E-7	7.4E-5
<input type="checkbox"/>	KEGG_PATHWAY	Signaling pathways regulating pluripotency of stem cells	RT		35	1.8	7.6E-7	7.4E-5
<input type="checkbox"/>	KEGG_PATHWAY	Pathways in cancer	RT		88	4.5	7.9E-7	7.4E-5
<input type="checkbox"/>	KEGG_PATHWAY	Neurotrophin signaling pathway	RT		31	1.6	9.1E-7	7.4E-5
<input type="checkbox"/>	KEGG_PATHWAY	Prolactin signaling pathway	RT		21	1.1	8.0E-6	5.2E-4
<input type="checkbox"/>	KEGG_PATHWAY	Gastric cancer	RT		33	1.7	1.6E-5	7.6E-4
<input type="checkbox"/>	KEGG_PATHWAY	Proteoglycans in cancer	RT		41	2.1	1.7E-5	7.6E-4
<input type="checkbox"/>	KEGG_PATHWAY	Hippo signaling pathway	RT		34	1.7	1.9E-5	7.6E-4
<input type="checkbox"/>	KEGG_PATHWAY	MAPK signaling pathway	RT		52	2.7	3.7E-5	1.3E-3
<input type="checkbox"/>	KEGG_PATHWAY	mTOR signaling pathway	RT		33	1.7	4.2E-5	1.3E-3
<input type="checkbox"/>	KEGG_PATHWAY	Insulin signaling pathway	RT		30	1.5	5.2E-5	1.5E-3
<input type="checkbox"/>	KEGG_PATHWAY	Measles	RT		30	1.5	6.8E-5	1.8E-3
<input type="checkbox"/>	KEGG_PATHWAY	Chronic myeloid leukemia	RT		20	1.0	1.0E-4	2.5E-3
<input type="checkbox"/>	KEGG_PATHWAY	Human papillomavirus infection	RT		55	2.8	1.2E-4	2.8E-3
<input type="checkbox"/>	KEGG_PATHWAY	Renal cell carcinoma	RT		18	0.9	2.8E-4	6.1E-3
<input type="checkbox"/>	KEGG_PATHWAY	Pancreatic cancer	RT		19	1.0	3.2E-4	6.5E-3
<input type="checkbox"/>	KEGG_PATHWAY	Wnt signaling pathway	RT		32	1.6	3.7E-4	6.8E-3
<input type="checkbox"/>	KEGG_PATHWAY	PI3K-Akt signaling pathway	RT		56	2.9	3.8E-4	6.8E-3
<input type="checkbox"/>	KEGG_PATHWAY	Hepatitis B	RT		31	1.6	4.7E-4	8.1E-3
<input type="checkbox"/>	KEGG_PATHWAY	p53 signaling pathway	RT		18	0.9	5.7E-4	9.3E-3
<input type="checkbox"/>	KEGG_PATHWAY	Acute myeloid leukemia	RT		17	0.9	6.2E-4	9.5E-3
<input type="checkbox"/>	KEGG_PATHWAY	Cellular senescence	RT		29	1.5	1.2E-3	1.7E-2
<input type="checkbox"/>	KEGG_PATHWAY	AMPK signaling pathway	RT		24	1.2	1.3E-3	1.7E-2
<input type="checkbox"/>	KEGG_PATHWAY	Hepatitis C	RT		29	1.5	1.3E-3	1.7E-2
<input type="checkbox"/>	KEGG_PATHWAY	Small cell lung cancer	RT		20	1.0	1.3E-3	1.7E-2
<input type="checkbox"/>	KEGG_PATHWAY	Melanoma	RT		17	0.9	1.4E-3	1.8E-2
<input type="checkbox"/>	KEGG_PATHWAY	Colorectal cancer	RT		19	1.0	1.5E-3	1.8E-2
<input type="checkbox"/>	KEGG_PATHWAY	Hepatocellular carcinoma	RT		30	1.5	1.8E-3	2.1E-2
<input type="checkbox"/>	KEGG_PATHWAY	FoxO signaling pathway	RT		25	1.3	2.0E-3	2.2E-2
<input type="checkbox"/>	KEGG_PATHWAY	Salmonella infection	RT		40	2.0	2.2E-3	2.4E-2
<input type="checkbox"/>	KEGG_PATHWAY	Prostate cancer	RT		20	1.0	2.6E-3	2.7E-2
<input type="checkbox"/>	KEGG_PATHWAY	Sphingolipid signaling pathway	RT		23	1.2	2.6E-3	2.7E-2
<input type="checkbox"/>	KEGG_PATHWAY	Central carbon metabolism in cancer	RT		16	0.8	2.9E-3	2.8E-2
<input type="checkbox"/>	KEGG_PATHWAY	Axon guidance	RT		31	1.6	3.2E-3	3.1E-2
<input type="checkbox"/>	KEGG_PATHWAY	Non-small cell lung cancer	RT		16	0.8	3.8E-3	3.5E-2
<input type="checkbox"/>	KEGG_PATHWAY	Focal adhesion	RT		33	1.7	4.2E-3	3.7E-2
<input type="checkbox"/>	KEGG_PATHWAY	HIF-1 signaling pathway	RT		21	1.1	4.4E-3	3.8E-2
<input type="checkbox"/>	KEGG_PATHWAY	Rap1 signaling pathway	RT		34	1.7	4.5E-3	3.8E-2
<input type="checkbox"/>	KEGG_PATHWAY	Autophagy - animal	RT		25	1.3	5.3E-3	4.4E-2
<input type="checkbox"/>	KEGG_PATHWAY	Apoptosis	RT		24	1.2	6.7E-3	5.5E-2
<input type="checkbox"/>	KEGG_PATHWAY	Yersinia infection	RT		24	1.2	7.4E-3	5.7E-2
<input type="checkbox"/>	KEGG_PATHWAY	Basal cell carcinoma	RT		14	0.7	7.4E-3	5.7E-2
<input type="checkbox"/>	KEGG_PATHWAY	Regulation of actin cytoskeleton	RT		34	1.7	7.9E-3	6.0E-2
<input type="checkbox"/>	KEGG_PATHWAY	Endometrial cancer	RT		13	0.7	9.7E-3	7.1E-2
<input type="checkbox"/>	KEGG_PATHWAY	Inositol phosphate metabolism	RT		15	0.8	1.1E-2	7.8E-2
<input type="checkbox"/>	KEGG_PATHWAY	Cell cycle	RT		22	1.1	1.1E-2	7.8E-2
<input type="checkbox"/>	KEGG_PATHWAY	C-type lectin receptor signaling pathway	RT		19	1.0	1.2E-2	8.0E-2
<input type="checkbox"/>	KEGG_PATHWAY	T cell receptor signaling pathway	RT		19	1.0	1.2E-2	8.0E-2
<input type="checkbox"/>	KEGG_PATHWAY	Type II diabetes mellitus	RT		11	0.6	1.2E-2	8.0E-2
<input type="checkbox"/>	KEGG_PATHWAY	Longevity regulating pathway	RT		17	0.9	1.2E-2	8.0E-2

Figure S5. KEGG pathway analysis using predicted gene targets of deregulated microRNAs in SCCC. The predicted gene targets of miR-383-5p, miR-424-5p and miR-508-3p, all deregulated in SCCC versus healthy control tissue, were downloaded from TargetScan (release 8.0; <https://www.targetscan.org>). The genes were subsequently used as input for the database for annotation, visualization and integrated discovery (DAVID- 2021 update; <https://david.ncifcrf.gov>) for a KEGG pathways analysis. Listed are the top 50 most significant pathways.