A *BAP1* Mutation-specific MicroRNA Signature Predicts Clinical Outcomes in Clear Cell Renal Cell Carcinoma Patients With Wild-type *BAP1*

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Short Running Title: *BAP1* Mutation and MicroRNAs in ccRCC

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Table S1. **Mutation status of *BAP1* in 35 patients with clear cell renal cell carcinoma**

Amino acid change	No.	Type	FIS	Validation
D311_splice	1	Splice		V
D407fs	1	FS del		V
D74fs	1	FS del		V
D75G	1	Missense	Neutral	V
E283fs	1	FS del		V
E31A3D	1	Missense	High	V
E54K	1	Missense	Low	I
F170C	1	Missense	High	V
F170V	1	Missense	High	V
G109V	1	Missense	High	V
G128*	1	Nonsense		V
G23_splice3D	1	Splice		V
G41_splice	1	Splice		V
I662N	1	Missense	Low	V
K626*	1	Nonsense		V
K711fs	1	FS del		V
L17P3D	1	Missense	Medium	I
L49V	1	Missense	High	I
M1I	2	Missense		I
M1V	1	Missense		I
N229H	1	Missense	Medium	V
N78S	2	Missense	Neutral	V
Q156*	1	Nonsense		V
Q253*	1	Nonsense		V
Q40*	1	Nonsense		V
R60*	1	Nonsense		V
R699fs	1	FS del		V
R717fs	1	FS del		V
S279*	1	Nonsense		V
S460*	1	Nonsense		V
V335fs	1	FS del		I
V77fs	1	FS del		V
Y627*	1	Nonsense		V

BAP1, *BRCA1 associated protein-1*; No., number; FIS, Functional Impact Score for the missense mutations (via Mutation Assessor); FS del, frame-shift deletion; V, validated; I, invalidated.

Table S2. **Univariate and multivariate analysis of parameters associated with overall survival in 350 ccRCC patients**

Variables	HR	95% CI	*P* value
Univariate Cox regression analysis			
Age (≥ 60 vs. <60)	2.699	1.772-4.111	<0.001
Gender (male vs. female)	0.749	0.512-1.095	0.136
Ethnicity (Caucasians vs. non-Caucasians)	1.446	0.458-4.561	0.530
AJCC stage (Ⅲ+Ⅳ vs. Ⅰ+Ⅱ)	4.890	3.158-7.571	<0.001
Tumor size (T3+T4 vs. T1+T2)	3.489	2.345-5.192	<0.001
Metastasis status (M1 vs. M0)	4.674	3.185-6.858	<0.001
Fuhrman grade (G3+G4 vs. G1+G2)	2.686	1.706-4.230	<0.001
Surgical type (RN vs. PN)	4.098	1.799-9.335	0.001
BAP1 status (Mutant vs. Wild-type)	1.909	1.175-3.102	0.009
Multivariate Cox regression analysis [a]			
Age (≥ 60 vs. <60)	2.148	1.402-3.291	<0.001
AJCC stage (Ⅲ+Ⅳ vs. Ⅰ+Ⅱ)	2.533	1.504-4.267	<0.001
Metastasis status (M1 vs. M0)	2.495	1.606-3.875	<0.001

ccRCC, clear cell renal cell carcinoma; HR, hazard ratio; CI, confidential interval; AJCC, AJCC, American Joint Committee on Cancer; RN, radical nephrectomy; PN, partial nephrectomy; *BAP1*, *BRCA1 associated protein-1*.

[a] The final results after stepwise analysis with Backward (LR) method

Table S3. **Summary of miRNAs expressed differentially between *BAP1* mutant and wild-type tumors**

MicroRNA	Expression Level [a]		Fold Change [b]	*P* value	FDR
	WT (n=315)	MUT (n=35)			
hsa-miR-653	5.99 ± 1.77	4.97 ± 1.45	0.49	0.0010523	0.0122
hsa-miR-100	11.70 ± 1.14	10.83 ± 1.49	0.55	4.26E-05	0.000898
hsa-miR-3074	3.11 ± 0.82	2.29 ± 0.90	0.56	< 1e-07	5.80E-06
hsa-miR-139	6.57 ± 1.13	5.78 ± 1.17	0.58	0.0001043	0.00186
hsa-miR-10b	17.35 ± 0.64	16.63 ± 0.64	0.61	< 1e-07	< 1e-07
hsa-miR-126	13.52 ± 0.86	12.84 ± 0.98	0.63	1.58E-05	0.000407
hsa-miR-503	5.04 ± 1.31	4.38 ± 1.26	0.63	0.0042028	0.0348
hsa-miR-1468	3.16 ± 0.90	2.53 ± 0.93	0.65	9.72E-05	0.00186
hsa-miR-181d	3.23 ± 0.90	2.63 ± 1.26	0.66	0.0003426	0.00497
hsa-miR-424	8.55 ± 1.11	7.95 ± 1.01	0.66	0.0022575	0.0218
hsa-miR-10a	14.53 ± 0.71	13.94 ± 0.63	0.66	3.10E-06	0.00012
hsa-miR-181b-2	2.51 ± 0.77	1.93 ± 0.83	0.67	3.25E-05	0.000754
hsa-miR-362	3.36 ± 0.88	2.78 ± 0.85	0.67	0.0002722	0.00421
hsa-miR-181a-1	10.56 ± 0.50	10.06 ± 0.78	0.70	2.00E-07	9.28E-06
hsa-miR-181a-2	9.59 ± 0.55	9.14 ± 0.75	0.73	1.31E-05	0.00038
hsa-miR-181b-1	8.30 ± 0.59	7.90 ± 0.92	0.76	0.0003929	0.00506
hsa-miR-125a	9.68 ± 0.52	9.34 ± 0.62	0.79	0.0003858	0.00506
hsa-miR-99b	15.02 ± 0.51	14.77 ± 0.56	0.84	0.0068379	0.0512
hsa-let-7i	9.00 ± 0.48	9.25 ± 0.53	1.19	0.0030514	0.0283
hsa-miR-30e	14.06 ± 0.49	14.32 ± 0.55	1.20	0.0031995	0.0285
hsa-miR-374a	9.73 ± 0.49	10.03 ± 0.35	1.23	0.0005426	0.00663
hsa-miR-22	15.89 ± 0.55	16.20 ± 0.53	1.25	0.0012788	0.0141
hsa-miR-29b-2	8.38 ± 0.65	8.70 ± 0.90	1.25	0.0079739	0.0561
hsa-miR-1307	9.68 ± 0.65	10.02 ± 0.63	1.27	0.0037618	0.0323
hsa-miR-1301	3.32 ± 0.72	3.68 ± 0.81	1.28	0.0060719	0.0486
hsa-miR-21	17.29 ± 0.66	17.71 ± 0.45	1.35	0.0002278	0.00377
hsa-miR-671	1.95 ± 0.89	2.39 ± 0.95	1.35	0.006821	0.0512
hsa-miR-365-1	4.86 ± 0.88	5.36 ± 0.91	1.41	0.0014623	0.0154
hsa-miR-365-2	4.86 ± 0.92	5.37 ± 0.90	1.41	0.0021703	0.0218
hsa-miR-200c	4.67 ± 1.10	5.19 ± 0.94	1.45	0.007096	0.0514
hsa-miR-149	2.67 ± 1.18	3.64 ± 1.24	1.96	1.02E-05	0.000338
hsa-miR-182	11.07 ± 1.43	12.91 ± 1.44	3.57	< 1e-07	< 1e-07
hsa-miR-183	8.97 ± 1.49	10.91 ± 1.49	3.85	< 1e-07	< 1e-07

BAP1, BRCA1 associated protein-1; WT, wild-type; MUT, mutant; FDR, false discovery rate.

[a] log2 transformed expression data

[b] geometric mean of the ratio between miRNAs derived from *BAP1* mutant and wild-type tumors

Table S4. **miRNAs associated with overall survival of ccRCC patients with wild-type *BAP1***

MicroRNA	HR	95% CI	Coefficient (*B*)	*P* value [a]
hsa-miR-10b	0.555	0.363-0.849	-0.588	0.007
hsa-miR-139	0.387	0.247-0.607	-0.949	< 0.001
hsa-miR-181a-2	0.608	0.399-0.926	-0.497	0.02
hsa-miR-149	1.701	1.110-2.607	0.531	0.015
hsa-miR-29b-2	1.876	1.221-2.882	0.629	0.004
hsa-miR-182	1.937	1.262-2.975	0.661	0.002
hsa-miR-183	2.046	1.327-3.156	0.716	0.001
hsa-miR-21	2.092	1.356-3.228	0.738	0.001
hsa-miR-365-2	2.178	1.393-3.406	0.778	0.001
hsa-miR-671	2.321	1.492-3.612	0.842	<0.001
hsa-miR-365-1	2.462	1.559-3.886	0.901	<0.001

ccRCC, clear cell renal cell carcinoma; *BAP1*, *BRCA1 associated protein-1*; HR, hazard ratio; CI, confidential interval;

[a] *P* values generated by univariate Cox regression analysis