BAP1 is Over-Expressed in Black vs. White Patients with Mx-M1 Clear Cell Renal Cell Carcinoma (ccRCC)

David J. Paulucci; John P. Sfakianos; Shalini Singh Yadav; Ketan K. Badani

Icahn School of Medicine at Mount Sinai Hospital, New York, NY

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Presenting Author: David J. Paulucci

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Introduction and Objectives: Incidence of renal cell carcinoma (RCC) is higher in Black patients with worse survival compared to White patients despite renal tumors among Blacks tending to be more localized. Studies attribute these disparities to higher rates of obesity, hypertension and a lack of access to quality health care in Blacks. With scant genomic evidence to account for these disparities, the present study compared BAP1 gene-level expression between Blacks and Whites with ccRCC; a gene that inhibits tumor progression when overexpressed, and when silenced results in poor clinical outcomes.

Methods: The Cancer Genome Atlas (TCGA) data set was used to identify 58 (9.9%) Black and 529 (90.9%) White patients with ccRCC. BAP1 expression was compared using a Mann-Whitney U test. The association between BAP1 expression and pathologic stage, AJCC stage, Fuhrman grade and OS was assessed for the overall cohort and stratified by race using linear regression models and Cox proportion hazards models adjusting for Fuhrman grade, pathologic stage and the presence of pathologic metastases for the overall cohort and stratified by race.

Results: The level of BAP1 expression was significantly higher in Black vs. White patients (10.5 vs. 10.3; $p<.001$) (Table 1). For the overall cohort, increasing BAP1 expression was associated with decreasing pathologic stage (β=-0.25, p=.004) and decreasing AJCC Stage (β=-.029, p=.006). For Black patients, increasing BAP1 expression was associated with decreasing AJCC stage (β=-0.79, p=.016), decreasing Fuhrman grade (β=-0.55, p=.011) and a decreased risk of pathologic metastases (OR=0.83, p=.038). For White patients, increasing BAP1 expression was associated with decreasing pathologic stage (β=-0.20, p=.026).

Conclusions: BAP1 is overexpressed in Black compared to White patients and is associated with favorable stage. This finding may explain why tumors among Black patients are more likely to be localized. BAP1 overexpression portends distinct clinical outcomes in Black and White patients demonstrating the need for racial stratification and adequate Black patient sampling in BAP1 biomarker studies.

Table 1. Clinical and Pathologic Characteristics of White and Black Patients with MX-M1 ccRCC

Characteristic	*White*	*Black or African American*	*P Value*
Patients	529 (90.1%)	58 (9.9%)	
Level of BAP1 Expression	10.3 (10.1-10.5)	10.5 (10.2-10.7)	**<.001**
Year of Initial Pathologic Diagnosis	2006 (2004-2007)	2010 (2006-2012)	**<.001**
Age	61.0 (52.0-70.0)	60 (53.0-68.3)	.523
Gender			
Male	359 (67.9 %)	28 (48.3%)	**.003**
Female	170 (32.1%)	30 (51.7%)	
Clinical M1	0 (0.0%)	3 (5.2%)	**<.001**
Pathologic M1	93 (17.6%)	5 (8.6%)	.082
Pathologic N1	18 (3.4%)	0 (0.0%)	.154
Pathologic T Stage	pT2 (pT1-pT3)	pT1 (pT1-pT2)	**<.001**
pT1	253 (47.8%)	40 (69.0%)	
pT2	69 (13.0%)	10 (17.2%)	
pT3	194 (36.7%)	8 (13.8%)	
pT4	13 (2.5%)	0 (0.0%)	
AJCC Stage	Stage 2 (Stage 1-Stage 3)	Stage 1 (Stage 1-Stage 2)	**.003**
Stage I	247 (46.7%)	40 (69.0%)	
Stage II	59 (11.2%)	5 (8.6%)	
Stage III	128 (24.2%)	6 (10.3%)	
Stage IV	95 (18.0%)	7 (12.1%)	
Fuhrman Grade	3 (1-3)	2 (2-3)	**.017**

Median Follow-Up	34.3 (11.7-58.4)	9.4 (1.4-37.2)	**<.001**

For categorical variables, chi square tests performed. Frequencies presented with percentages in parenthesis.

For continuous variables, Mann-Whitney U tests performed. Medians presented with Interquartile Ranges in parenthesis.