Supplementary Data

Figure S1. Kaplan-Meier Analysis of overall survival and disease specific survival in the separated MVAC discovery and Gem/Cis validation cohorts of patients with mutations in in ATM, RB1, FANCC (Mutant) versus those without a mutation in these genes (Wild Type).

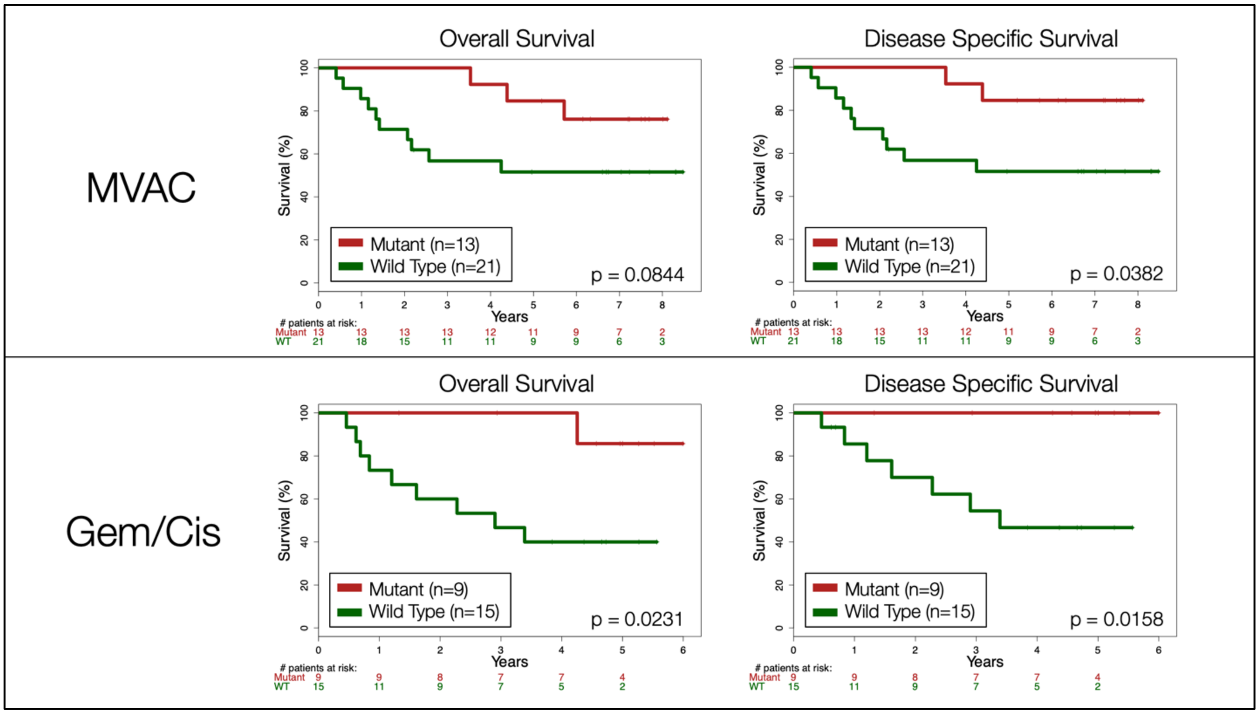
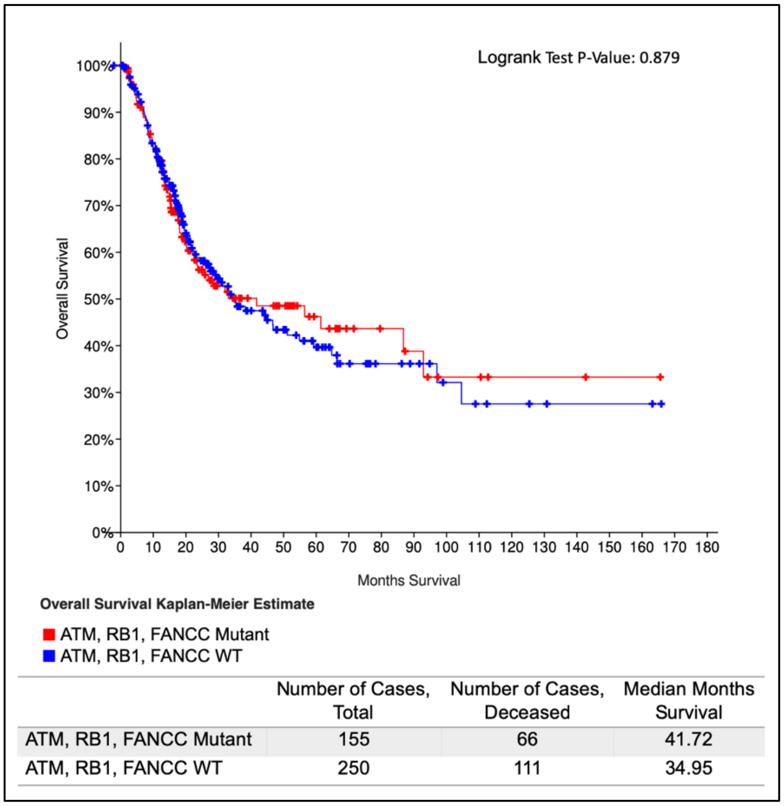


Figure S2. Overall Survival Kaplan-Meier Estimate generated via cBioPortal of patients with muscle invasive bladder cancer with mutations in ATM, RB1, FANCC compared to those without from the TCGA suggest no significant difference in overall survival in patients with a mutation when analyzed regardless of treatment. Of note, only a small number of patients (n=12) received neoadjuvant chemotherapy in this data set. (Robertson AG, Kim J, Al-ahmadie H, et al. Comprehensive Molecular Characterization of Muscle-Invasive Bladder Cancer. Cell. 2017;171(3):540-556.e25.)



	Number of Cases, Total	Number of Cases, Deceased	Median Months Survival
ATM, RB1, FANCC Mutant	155	66	41.72
ATM, RB1, FANCC WT	250	111	34.95

Table S1. Mutations listed by protein change, type of alteration and predicted functionality. A functional modeling score was designed to assess the potential biological consequence of alterations by using structural analysis and protein features and was compared to Polyphen2 score. These methodologies are published in the previous publication.[8]

ATM			**RB1**			**FANCC**		
Protein Mutation	**Mutation Type**	**Predicted Function**	**Protein Mutation**	**Mutation Type**	**Predicted Function**	**Protein Mutation**	**Mutation Type**	**Predicted Function**
Y2009H	Missense	Deleterious	R787*	Stop	Deleterious	L52F	Missense	Deleterious
D1563N	Missense	Deleterious	Loss	Loss	Deleterious	R185*	Stop	Deleterious
R3008C	Missense	Deleterious	F216fs*7	Stop	Deleterious	I312V	Missense	Deleterious
L3035F	Missense	Deleterious	S862G	Missense	Neutral	E539K	Missense	Deleterious
L1019V,	Missense	Deleterious	Splice 920	Splice	Deleterious			
K2413Q	Missense	Neutral	L665V	Missense	Deleterious			
R2580K	Missense	Deleterious	R455*	Stop	Deleterious			
L1419fs*4	Stop	Deleterious	R787fs*23	Stop	Deleterious			
R337H	Missense	Deleterious	S360fs*2	Stop	Deleterious			
E2895K	Missense	Deleterious	Splice	Splice	Deleterious			
E2932D	Missense	Deleterious	G801E	Missense	Deleterious			
D1791N	Missense	Neutral	D1791N	Missense	Deleterious			
Splice 17	Splice	Deleterious	P595fs*47	Stop	Deleterious			
R2443Q	Missense	Deleterious	Q444H	Missense	Deleterious			
E1325K	Missense	Deleterious	E492K	Missense	Deleterious			

Table S2. Incidence of mutations in ATM, RB1 and FANCC in the cohort of patients sequenced for this study (n=58) as compared to the muscle invasive bladder cancer cohort from the TCGA (n= 408) queried via cBioPortal.

	Combined Study Cohort (n = 58)	TCGA Cohort (n = 408)
ATM	19% (11/58)	15%
RB1	19% (11/58)	25%
FANCC	7% (4/58)	2.9%