

Table 1. Characteristics of subjects after excluding subjects with missing values[#]

	NMIBC (n = 601)	MIBC (n = 77)	All (n = 678)
Age			
Median (Q1, Q3)	66 (57,71)	67 (59,72)	66 (58,71)
Hannum Age Acceleration			
Median (Q1, Q3)	-0.25 (-3.41,3.06)	-0.91 (-3.46,1.33)	-0.32 (-3.41,2.87)
Sex			
Male	455 (75.7%)	56 (72.7%)	511 (75.4%)
Female	146 (24.3%)	21 (27.3%)	167 (24.6%)
Tumor grade			
Grade 1	289 (48.1%)	2 (2.6%)	291 (42.9%)
Grade 2	161 (26.8%)	11 (14.3%)	172 (25.4%)
Grade 3	125 (20.8%)	29 (37.7%)	154 (22.7%)
Grade 4	26 (4.3%)	35 (45.5%)	61 (9.0%)
Smoking status			
Never	103 (17.1%)	16 (20.8%)	119 (17.6%)
Ever	498 (82.9%)	61 (79.2%)	559 (82.4%)
BCG: Immunotherapy			
No	512 (85.2%)	72 (93.5%)	587 (86.6%)
Yes	89 (14.8%)	2 (6.5%)	91 (13.4%)
NLR			
Median (Q1, Q3)	1.96 (1.38, 2.86)	2.24 (1.55, 3.67)	1.99 (1.40, 2.97)
10-year dead status			
Alive	423 (70.4%)	27 (35.1%)	450 (66.4%)
Deceased	178 (29.6%)	50 (64.9%)	228 (33.6%)
10-year Recurrence-free status*			
No	230 (38.3%)	19 (24.7%)	249 (36.7%)
Yes	371 (61.7%)	58 (75.3%)	429 (63.3%)

[#]: Exclude subjects with missing values in muscle-invasive status, pathology reviewing status, tumor grade, or smoking status

*: whether patient with tumor recurrence or deceased within 10 years.

Table 2. Cox proportional hazards multivariable models for patient and tumor characteristics

	10-year overall survival			10-year recurrence-free survival		
	HR (95% CI)			HR (95% CI)		
	NMIBC + MIBC [#] (N = 678)	NMIBC (N = 601)	MIBC (N = 77)	NMIBC + MIBC [§] (N = 678)	NMIBC ^{&} (N = 601)	MIBC (N = 77)
Age	1.08 (1.06-1.10)	1.08 (1.06-1.11)	1.06 (1.01-1.11)	1.37 (1.12-1.69)	1.02 (1.00-1.03)	1.04 (1.00-1.08)
Hannum Age Acceleration	1.03 (1.00-1.06)	1.06 (1.02-1.09)	0.96 (0.91-1.03)	0.98 (0.96-1.01)	1.00 (0.98-1.02)	0.95 (0.90-1.01)
Sex						
Male	Referent group					
Female	0.49 (0.34-0.72)	0.54 (0.35-0.84)	0.38 (0.18-0.79)			0.64 (0.33-1.25)
Tumor grade						
1 + 2	Referent group					
3 + 4	1.45 (1.07-1.95)	1.55 (1.12-2.13)	1.20 (0.55-2.59)	1.34 (1.06-1.68)	1.46 (1.16-1.85)	0.71 (0.35-1.46)
Smoking status						
Non-smoker	Referent group					
Ever-smoker	1.41 (0.95-2.10)	1.64 (1.02-2.64)	0.91 (0.43-1.94)	1.58 (1.19-2.09)	1.65 (1.21-2.25)	1.09 (0.53-2.22)
BCG treatment						
No	Referent group					
Yes	0.87 (0.58-1.31)	0.88 (0.58-1.33)	0.65 (0.09-4.87)			1.42 (0.32-6.33)

NMIBC: non-muscle-invasive bladder cancer, MIBC: muscle-invasive bladder cancer, HR: hazard ratio, CI: confidence interval

[#]: Stratification was used on muscle-invasive status for proportional assumption.

[§]: For proportional assumption, Stratification was used on sex, muscle-invasive status, and BCG treatment status, and age was a categorical variable based on median level (referent group: Age ≤ 65).

[&]: Stratification was used on sex and BCG treatment status for proportional assumption.

Table 3. Cox proportional hazards models of immune cell proportions and bladder cancer patient outcomes

	10-year overall survival				10-year recurrence-free survival			
	Univariate model		Multivariable [§] model		Univariate model		Multivariable [#] model	
	HR (95% CI)	P value	HR	FDR	HR (95% CI)	P value	HR	FDR
NLR	1.35 (1.27-1.43)	5.9E-23	1.25	6.8E-10	1.12 (1.06-1.17)	1.8E-5	1.11	0.003
Memory B cell	0.80 (0.70-0.92)	1.3E-3	0.89	0.09	0.91 (0.84-1.00)	0.047	0.96	0.38
Naïve B cell	0.84 (0.78-0.91)	3.2E-6	0.91	0.02	0.98 (0.93-1.02)	0.30		
Memory CD4T cell	0.93 (0.90-0.95)	2.2E-8	0.97	0.02	0.97 (0.96-0.99)	3.0E-3	0.98	0.06
Naïve CD4T cell	0.88 (0.84-0.93)	5.3E-6	0.96	0.14	0.96 (0.92-0.99)	6.5E-3	0.98	0.27
Memory CD8T cell	0.96 (0.94-0.99)	3.3E-3	0.94	5.1E-5	0.99 (0.97-1.00)	0.11		
Naïve CD8T cell	0.83 (0.75-0.91)	1.1E-4	1.06	0.29	0.92 (0.86-0.98)	9.8E-3	0.99	0.78
Monocyte	1.04 (1.00-1.09)	0.06			1.05 (1.02-1.08)	3.2E-3	1.04	0.06
Neutrophil	1.05 (1.04-1.06)	1.0E-14	1.04	5.6E-7	1.01 (1.00-1.02)	5.7E-3	1.01	0.08
Regulatory T cell	1.00 (0.89-1.14)	0.95			1.02 (0.94-1.12)	0.60		
NK cell	0.92 (0.87-0.98)	6.2E-3	0.91	0.008	0.98 (0.94-1.02)	0.35		
Basophil	1.03 (0.94-1.14)	0.50			1.02 (0.95-1.09)	0.66		
Eosinophil	0.99 (0.93-1.06)	0.75			1.02 (0.97-1.07)	0.47		

HR: hazard ratio, CI: confidence interval, NLR: neutrophil to lymphocyte ratio

Winsorization was used on the top 2% values for fitting linearity assumption.

§: The model controlling for age, sex, stratified muscle-invasive status, tumor grade, smoking status, BCG treatment status, age acceleration.

#: The model controlling for age, stratified sex, stratified muscle-invasive status, tumor grade, smoking status, stratified BCG treatment status.

Table 3. Cox proportional hazards models of immune cell proportions and bladder cancer patient outcomes

	10-year overall survival			10-year recurrence-free survival		
	Univariate model	Multivariable [§] model		Univariate model	Multivariable [#] model	
	HR (95% CI)	HR (95% CI)	FDR	HR (95% CI)	HR (95% CI)	FDR
NLR	1.43 (1.33-1.54)	1.31 (1.21-1.42)	1.0E-9	1.14 (1.07-1.21)	1.12 (1.05-1.20)	3.8E-3
Memory B cell	0.82 (0.73-0.93)	0.88 (0.78-0.99)	0.04	0.94 (0.87-1.01)		
Naïve B cell	0.84 (0.78-0.91)	0.93 (0.86-1.00)	0.07	0.98 (0.94-1.03)		
Memory CD4T cell	0.93 (0.91-0.95)	0.96 (0.94-0.99)	0.01	0.97 (0.96-0.99)	0.98 (0.96-0.99)	0.02
Naïve CD4T cell	0.89 (0.85-0.94)	0.98 (0.93-1.03)	0.42	0.95 (0.92-0.99)	0.97 (0.94-1.01)	0.13
Memory CD8T cell	0.97 (0.94-0.99)	0.95 (0.92-0.97)	3.6E-5	0.99 (0.97-1.01)		
Naïve CD8T cell	0.85 (0.75-0.95)	1.20 (1.04-1.38)	0.01	0.93 (0.86-1.01)		
Monocyte	1.06 (1.02-1.10)	1.03 (0.98-1.07)	0.25	1.05 (1.02-1.09)	1.04 (1.01-1.08)	0.01
Neutrophil	1.05 (1.04-1.07)	1.04 (1.03-1.05)	2.4E-7	1.01 (1.00-1.02)	1.01 (1.00-1.02)	5.1E-2
Regulatory T cell	1.25 (1.09-1.45)	1.27 (1.10-1.47)	3.7E-3	1.20 (1.07-1.34)	1.19 (1.06-1.33)	0.01
NK cell	0.94 (0.89-0.99)	0.92 (0.87-0.97)	7.3E-3	0.99 (0.95-1.02)		
Basophil	1.45 (1.21-1.74)	1.31 (1.09-1.58)	7.3E-3	1.19 (1.03-1.37)	1.18 (1.02-1.36)	0.04
Eosinophil	1.01 (0.94-1.07)			1.02 (0.98-1.07)		

HR: hazard ratio, CI: confidence interval, NLR: neutrophil to lymphocyte ratio

Winsorization was used on the top 2% values or the last 2% (only Neu) for fitting linearity assumption.

§: The model controlling for age, sex, stratified muscle-invasive status, tumor grade, smoking status, BCG treatment status, and age acceleration.

#: The model controlling for age, stratified sex, stratified muscle-invasive status, tumor grade, smoking status, stratified BCG treatment status, and age acceleration.

Table 4. Cox proportional hazards models of immune cell proportions and NMIBC patient outcomes

	10-year overall survival				10-year recurrence-free survival			
	Univariate model		Multivariable [§] model		Univariate model		Multivariable [#] model	
	HR (95% CI)	P value	HR	FDR	HR (95% CI)	P value	HR	FDR
NLR	1.39 (1.30-1.48)	5.7E-21	1.32	1.3E-11	1.11 (1.05-1.18)	1.6E-4	1.10	0.01
Memory B cell	0.81 (0.69-0.94)	5.9E-3	0.89	0.13	0.92 (0.84-1.01)	0.08		
Naïve B cell	0.84 (0.77-0.91)	2.4E-5	0.90	0.02	0.98 (0.94-1.03)	0.45		
Memory CD4T cell	0.93 (0.90-0.95)	4.9E-7	0.96	0.02	0.97 (0.96-0.99)	5.3E-3	0.98	0.08
Naïve CD4T cell	0.85 (0.80-0.91)	1.1E-6	0.92	0.03	0.95 (0.92-0.99)	6.4E-3	0.97	0.20
Memory CD8T cell	0.96 (0.93-0.99)	3.9E-3	0.94	1.3E-4	0.99 (0.97-1.01)	0.29		
Naïve CD8T cell	0.82 (0.73-0.91)	2.3E-4	1.05	0.45	0.92 (0.86-0.99)	0.02	0.99	0.79
Monocyte	1.04 (0.99-1.10)	0.09			1.04 (1.01-1.08)	0.01	1.03	0.11
Neutrophil	1.06 (1.04-1.07)	1.9E-14	1.04	1.1E-7	1.01 (1.00-1.02)	0.01	1.01	0.11
Regulatory T cell	0.95 (0.81-1.11)	0.49			1.02 (0.93-1.12)	0.67		
NK cell	0.90 (0.84-0.96)	2.3E-3	0.89	1.5E-3	0.97 (0.93-1.02)	0.20		
Basophil	1.02 (0.91-1.14)	0.73			1.02 (0.94-1.10)	0.64		
Eosinophil	1.01 (0.94-1.09)	0.81			1.02 (0.97-1.07)	0.47		

HR: hazard ratio, CI: confidence interval, NLR: neutrophil to lymphocyte ratio

Winsorization was used on the top 2% values for fitting linearity assumption.

§: The model controlling for age, sex, tumor grade, smoking status, BCG treatment status, age acceleration.

#: The model controlling for age, stratified sex, tumor grade, smoking status, stratified BCG treatment status.

Table 4. Cox proportional hazards models of immune cell proportions and NMIBC patient outcomes

	10-year overall survival			10-year recurrence-free survival		
	Univariate model	Multivariable [§] model		Univariate model	Multivariable [#] model	
	HR (95% CI)	HR (95% CI)	FDR	HR (95% CI)	HR (95% CI)	FDR
NLR	1.49 (1.37-1.62)	1.41 (1.28-1.55)	1.5E-11	1.14 (1.06-1.22)	1.12 (1.04-1.21)	0.01
Memory B cell	0.82 (0.72-0.94)	0.86 (0.75-0.99)	0.04	0.94 (0.87-1.03)		
Naïve B cell	0.86 (0.79-0.94)	0.94 (0.86-1.02)	0.15	0.99 (0.94-1.04)		
Memory CD4T cell	0.92 (0.90-0.95)	0.95 (0.93-0.98)	1.9E-3	0.97 (0.96-0.99)	0.98 (0.96-0.99)	0.01
Naïve CD4T cell	0.87 (0.82-0.93)	0.96 (0.90-1.02)	0.21	0.95 (0.92-0.99)	0.97 (0.93-1.01)	0.13
Memory CD8T cell	0.96 (0.94-0.99)	0.94 (0.91-0.97)	1.1E-4	0.99 (0.97-1.01)		
Naïve CD8T cell	0.84 (0.73-0.96)	1.20 (1.03-1.40)	0.03	0.93 (0.86-1.02)		
Monocyte	1.06 (1.02-1.11)	1.03 (0.98-1.08)	0.28	1.05 (1.02-1.08)	1.04 (1.01-1.07)	0.02
Neutrophil	1.06 (1.05-1.08)	1.05 (1.03-1.07)	4.7E-8	1.01 (1.00-1.02)	1.01 (1.00-1.02)	0.07
Regulatory T cell	1.27 (1.08-1.49)	1.28 (1.09-1.51)	5.6E-3	1.20 (1.06-1.35)	1.19 (1.06-1.34)	0.01
NK cell	0.92 (0.87-0.98)	0.90 (0.84-0.96)	1.9E-3	0.98 (0.94-1.02)		
Basophil	1.51 (1.24-1.85)	1.36 (1.10-1.68)	6.9E-3	1.16 (0.99-1.35)		
Eosinophil	1.02 (0.95-1.10)			1.03 (0.98-1.08)		

HR: hazard ratio, CI: confidence interval, NLR: neutrophil to lymphocyte ratio

Winsorization was used on the top 2% or the last 2% (only Neu) values for fitting linearity assumption.

§: The model controlling for age, sex, tumor grade, smoking status, BCG treatment status, and age acceleration.

#: The model controlling for age, stratified sex, tumor grade, smoking status, stratified BCG treatment status, and age acceleration.

Supplemental Table 1. Cox proportional hazards models of immune cell proportions and MIBC patient outcomes

	10-year overall survival			10-year recurrence-free survival		
	Univariate model		P-value	Univariate model		FDR
	HR (95% CI)	HR (95% CI)		HR (95% CI)	HR (95% CI)	
NLR	1.12 (0.96-1.31)	1.09 (0.93-1.27)	0.30	1.10 (0.95-1.27)	1.06 (0.91-1.22)	0.47
Memory B cell	0.91 (0.70-1.18)			0.91 (0.72-1.15)		
Naïve B cell	0.86 (0.72-1.02)			0.95 (0.82-1.11)		
Memory CD4T cell	0.99 (0.95-1.03)			0.99 (0.96-1.03)		
Naïve CD4T cell	1.03 (0.93-1.14)			1.00 (0.91-1.10)		
Memory CD8T cell	0.97 (0.92-1.02)			0.96 (0.92-1.00)		
Naïve CD8T cell	0.99 (0.75-1.30)			0.95 (0.74-1.22)		
Monocyte	1.03 (0.94-1.12)			1.09 (1.01-1.18)	1.04 (0.95-1.13)	0.47
Neutrophil	1.01 (0.99-1.04)			1.01 (0.98-1.03)		
Regulatory T cell	1.31 (0.93-1.84)			1.22 (0.90-1.67)		
NK cell	1.03 (0.93-1.14)			1.05 (0.96-1.15)		
Basophil	1.24 (0.81-1.89)			1.43 (0.99-2.06)		
Eosinophil	0.97 (0.85-1.09)			1.01 (0.90-1.14)		

HR: hazard ratio, CI: confidence interval, NLR: neutrophil to lymphocyte ratio

Winsorization was used on the top 2% values for fitting linearity assumption.

\$: The model controlling for age, sex, tumor grade, smoking status, BCG treatment status, and age acceleration.

Supplemental Table 3. Cox proportional hazards models of immune cell profiles and bladder cancer patient outcomes

	10-year overall survival				10-year recurrence-free survival			
	Univariate model		Multivariable [§] model		Univariate model		Multivariable [#] model	
	HR (95% CI)	P value	HR	FDR	HR (95% CI)	P value	HR	FDR
CD4T	0.94 (0.92-0.96)	6.1E-10	0.97	2.5E-3	0.98 (0.96-0.99)	6.3E-4	0.99	0.08
CD8T	0.94 (0.92-0.97)	4.4E-5	0.94	1.0E-4	0.98 (0.96-1.00)	0.02	0.98	0.04
B cell	0.84 (0.79-0.90)	3.7E-8	0.90	2.1E-3	0.97 (0.93-1.01)	0.12		
Lymphocyte	0.95 (0.93-0.96)	1.2E-15	0.96	4.0E-8	0.98 (0.98-0.99)	1.8E-4	0.99	0.04
Naïve cell	0.91 (0.89-0.94)	6.1E-9	0.96	0.02	0.97 (0.96-0.99)	0.01	1.00	0.69
NLR	1.35 (1.27-1.43)	5.9E-23	1.26	2.7E-11	1.12 (1.06-1.17)	1.8E-5	1.09	0.01
Lymph / Mono	0.89 (0.85-0.94)	4.6E-6	0.93	2.5E-3	0.96 (0.94-0.99)	1.8E-3	0.97	0.04
Bnv / Total Bcell	0.99 (0.99, 1.00)	1.5E-5	0.995	0.02	1.00 (1.00, 1.00)	0.39		
CD4T/CD8T	0.96 (0.89-1.04)	0.29			0.99 (0.94-1.04)	0.64		
CD4nv / Total CD4	0.98 (0.97, 0.99)	3.86E-5	0.99	0.08	0.99 (0.99, 1.00)	0.02	1.00	0.46
CD4nv / CD4mem	0.52 (0.34, 0.81)	0.004	0.76	0.17	0.77 (0.59, 1.01)	0.06		
CD8nv / Total CD8	1.00 (0.99, 1.00)	0.38			1.00 (0.99, 1.00)	0.42		
CD8nv / CD8mem	0.97 (0.82, 1.15)	0.73			0.98 (0.88, 1.11)	0.78		
CD8mem / Treg								
High		Referent Group				Referent Group		
Low	1.19 (0.92-1.55)	0.181			1.20 (0.99-1.45)	0.06		
Treg / Total CD4	1.01 (1.00, 1.02)	0.140			1.00 (1.00, 1.01)	0.30		
Naïve / Lymph	0.12 (0.04, 0.34)	6.8E-5	0.82	0.73	0.52 (0.25, 1.08)	0.08		

HR: hazard ratio, CI: confidence interval, NLR: neutrophil to lymphocyte ratio

Winsorization was used on the top 2% values for fitting linearity assumption.

§: The model controlling for age, sex, stratified muscle-invasive status, tumor grade, smoking status, BCG treatment status.

#: The model controlling for age, stratified sex, stratified muscle-invasive status, tumor grade, smoking status, stratified BCG treatment status.

Supplemental Table 2. Distributions of immune profiles

	NMIBC (n = 601)	MIBC (n = 77)	All (n = 678)
CD4T (%)			
Median (Q1, Q3)	11.8 (7.9, 17.4)	9.3 (4.8, 14.8)	11.7 (7.6, 17.0)
Min, Max	0.0, 49.7	0.0, 37.7	0.0, 49.7
CD8T (%)			
Median (Q1, Q3)	7.5 (4.7, 11.8)	7.3 (4.7, 9.0)	7.5 (4.7, 11.8)
Min, Max	0.0, 39.4	0.0, 29.2	0.0, 39.4
B cell (%)			
Median (Q1, Q3)	3.3 (1.7, 4.9)	2.5 (1.1, 4.1)	3.2 (1.6, 4.9)
Min, Max	0.0, 18.7	0.0, 11.9	0.0, 18.7
Lymphocyte (%)			
Median (Q1, Q3)	28.8 (21.6, 36.6)	25.1 (16.9, 33.9)	29.5 (21.0, 36.4)
Min, Max	2.7, 72.4	6.1, 60.9	2.7, 72.4
Naïve cell (%)			
Median (Q1, Q3)	5.4 (2.4, 9.7)	4.1 (0.8, 8.0)	5.2 (2.1, 9.5)
Min, Max	0.0, 32.1	0.0, 22.2	0.0, 32.1
NLR			
Median (Q1, Q3)	2.1 (1.5, 3.1)	2.5 (1.7, 4.1)	2.1 (1.5, 3.2)
Min, Max	0.2, 32.0	0.2, 13.4	0.2, 32.0
Lymphocyte / Monocyte			
Median (Q1, Q3)	3.8 (2.6, 5.8)	3.6 (2.0, 5.5)	3.8 (2.5, 5.8)
Min, Max	0.2, 2469.0	0.5, 38.7	0.2, 2469.0
B naïve / Total B cell (%)			
Median (Q1, Q3)	58.3 (28.5, 78.2)	46.8 (0.0, 87.1)	57.9 (21.8, 78.6)
Min, Max	0.0, 100.0	0.0, 100.0	0.0, 100.0
CD4T / CD8T			
Median (Q1, Q3)	1.6 (0.9, 2.6)	1.4 (0.5, 2.3)	1.6 (0.9, 2.5)
Min, Max	0.0, 3270.0	0.0, 136.0	0.0, 3270.0
CD4nv / Total CD4T (%)			
Median (Q1, Q3)	12.3 (0.0, 27.5)	4.9 (0.0, 24.6)	11.7 (0.0, 27.1)
Min, Max	0.0, 80.8	0.0, 63.8	0.0, 80.8
CD4T naïve / CD4T mem			
Median (Q1, Q3)	0.1 (0.0, 0.4)	0.1 (0.0, 0.4)	0.1 (0.0, 0.4)

Min, Max	0.0, 544.0	0.0, 61.0	0.0, 544.0
CD8nv / Total CD8T (%)			
Median (Q1, Q3)	16.8 (0.0, 36.3)	14.1 (0.0, 34.4)	16.6 (0.0, 36.1)
Min, Max	0.0, 100.0	0.0, 100.0	0.0, 100.0
CD8T naïve / CD8T mem			
Median (Q1, Q3)	0.2 (0.0, 0.6)	0.2 (0.0, 0.5)	0.2 (0.0, 0.6)
Min, Max	0.0, 690.0	0.0, 4.6	0.0, 690.0
Treg / Total CD4T (%)			
Median (Q1, Q3)	0.0 (0.0, 1.7)	0.0 (0.0, 5.1)	0.0 (0.0, 1.9)
Min, Max	0.0, 100.0	0.0, 100.0	0.0, 100.0
CD8T mem / Treg			
Median (Q1, Q3)	352.0 (17.2, 757.0)	310.0 (25.7, 603.0)	351.5 (17.4, 747.0)
Min, Max	0.0, 2481.0	0.0, 2923.0	0.0, 2923.0
Naïve / Lymphocyte			
Median (Q1, Q3)	0.2 (0.1, 0.3)	0.2 (0.0, 0.3)	0.2 (0.1, 0.3)
Min, Max	0.0, 0.6	0.0, 0.4	0.0, 0.6

Supplemental Table 2. Information of optimal 37 CpGs used in fitting RPM

Target gene name (UCSC)	Chromosome	The location relative to the CpG island	Gene region (UCSC)
ANKFN1	chr11	S_Shore	
	chr17	OpenSea	Body
	chr16	OpenSea	
RAB31	chr18	OpenSea	3'UTR
UBE2J2	chr1	OpenSea	Body
SLCO6A1	chr5	OpenSea	
	chr5	S_Shore	TSS200
	chr21	OpenSea	
SPRED2	chr2	OpenSea	1stExon
NR2F6	chr19	N_Shore	Body
ASGR2	chr17	OpenSea	Body
GORASP2	chr2	N_Shore	TSS200
ZBTB16	chr11	N_Shelf	Body
CLRN2	chr4	S_Shelf	Body
SUSD3	chr9	OpenSea	Body
B4GALT5	chr20	OpenSea	Body
TBXAS1	chr7	OpenSea	5'UTR
WWP2	chr16	OpenSea	Body
ZNF534	chr19	Island	3'UTR
MAPK14	chr6	OpenSea	Body
RGS12	chr12	OpenSea	
	chr4	OpenSea	Body
	chr1	OpenSea	Body
TCEA3	chr10	S_Shore	Body
DLG2	chr11	OpenSea	Body
NHEDC2	chr4	S_Shore	TSS200
ANKRD11	chr16	OpenSea	Body
MYOM2	chr8	N_Shore	Body
SPRED2	chr2	OpenSea	5'UTR
NDRG1	chr8	OpenSea	Body
CYTH4	chr22	OpenSea	Body
	chr19	OpenSea	

NAP1L4	chr11	N_Shore	5'UTR
IGF2R	chr6	OpenSea	Body
	chr17	OpenSea	
RBM47	chr4	OpenSea	5'UTR
ANKRD22	chr10	OpenSea	TSS200

Supplemental Table 2B. Overlapping CpGs with the EWAS result (10-year RFS) in previous paper [Chen et al., 2021]

CpG	Chromosome	Target gene name (UCSC)	The location relative to the CpG island	Gene region (UCSC)
cg20187292	chr21		OpenSea	
cg14352601	chr7	TBXAS1	OpenSea	5'UTR
cg04703221	chr16	WWP2	OpenSea	Body
cg09010707	chr12		OpenSea	

		partDSA		
		Group 1	Group 2	Group 3
SS-RPMM	rL	241 (40.1%)	17 (2.8%)	38 (6.3%)
	rR	213 (35.5%)	0 (0.0%)	92 (15.3%)

(Pheno_acc)		partDSA		
		Group 1	Group 2	Group 3
SS-RPMM	rL	154 (25.6%)	17 (2.8%)	26 (4.3%)
	rR	300 (50.0%)	0 (0.0%)	104 (17.3%)