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| **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. | | | |

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| **Table 2.** Cox proportional hazards multivariable models for patient and tumor characteristics | | | | | | |
|  | 10-year overall survival  HR (95% CI) | | | 10-year recurrence-free survival  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. | | | | | | |

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| **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. | | | | | | | | |

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| **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. | | | | | | |

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| **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. | | | | | | | | |

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| **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. | | | | | | |

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| **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 | Multivariable$ model | | Univariate model | Multivariable$ model | |
|  | HR (95% CI) | HR (95% CI) | P-value | HR (95% CI) | HR (95% CI) | FDR |
| 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. | | | | | | |

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| **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. | | | | | | | | |

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| **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 |

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| **Supplemental Table 2. Information of optimal 37 CpGs used in fitting RPMM** | | | |
| Target gene name (UCSC) | Chromosome | The location relative to the CpG island | Gene region (UCSC) |
|  | chr11 | S\_Shore |  |
| ANKFN1 | chr17 | OpenSea | Body |
|  | chr16 | OpenSea |  |
| RAB31 | chr18 | OpenSea | 3'UTR |
| UBE2J2 | chr1 | OpenSea | Body |
|  | chr5 | OpenSea |  |
| SLCO6A1 | 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 |
|  | chr12 | OpenSea |  |
| RGS12 | chr4 | OpenSea | Body |
| TCEA3 | chr1 | OpenSea | Body |
| ECHDC3 | 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%) |
|  | | | | |