

Table 1. Incorporation of EI-score gene expression information improves the established risk classifiers performance in MMRF dataset.

Multivariate model	Cox Proportional Hazard Regression				ML Model ROC-AUC		
Progression free survival (PFS)	Likelihood ratio test	Wald test	Score (logrank) test	Concordance (C-index)	Random-forest	gradient boosting	Negative binomial
1) mSMARTcyto	10.47	11.02	11.04	0.54	0.48	0.52	0.52
mSMARTcyto + APOBEC2, APOBEC3B	49.15	58.82	62.15	0.60	0.54	0.57	0.58
mSMARTcyto + IL11, TGFB1, TGFB3	24.19	24.64	24.87	0.58	0.55	0.56	0.57
mSMARTcyto + APOBEC + Cytokines	56.46	60.62	62.24	0.63	0.6	0.6	0.61
2) ISS	59.41	59.28	60.75	0.60	0.6	0.6	0.59
ISS + APOBEC2, APOBEC3B	79.16	87.18	90.55	0.63	0.62	0.63	0.63
ISS + IL11, TGFB1, TGFB3	52.04	51.97	52.98	0.62	0.61	0.62	0.61
ISS + APOBEC + Cytokines	96.22	103.5	107.7	0.65	0.62	0.65	0.65
3) R-ISS	36.92	36.91	37.05	0.60	0.55	0.55	0.54
R-ISS + APOBEC2, APOBEC3B	71.75	79.01	83.4	0.65	0.6	0.61	0.6
R-ISS + IL11, TGFB1, TGFB3	52.84	52.14	53.06	0.65	0.56	0.59	0.6
R-ISS + APOBEC + Cytokines	90.28	96.5	102.4	0.68	0.61	0.62	0.63
4) R-ISS-nocyto	38.58	38	38.46	0.60	0.58	0.59	0.59
R-ISS-nocyto + APOBEC2, APOBEC3B	77.63	85.04	90.72	0.66	0.65	0.67	0.67
R-ISS-nocyto + IL11, TGFB1, TGFB3	56.02	54.22	55.46	0.66	0.62	0.65	0.66
R-ISS-nocyto + APOBEC + Cytokines	92.5	97.33	104.8	0.69	0.66	0.69	0.68
5) blood parameters (β-2-microglobuline, LDH)	38.6	43.57	44.36	0.62	0.61	0.6	0.6
blood parameters* + APOBEC2, APOBEC3B	97.3	103	108.4	0.67	0.63	0.65	0.66
blood parameters* + IL11, TGFB1, TGFB3	70.43	69.52	71.11	0.66	0.63	0.64	0.65
blood parameters* + APOBEC + Cytokines (EI-score)	114.4	120.1	126.4	0.69	0.65	0.67	0.66
6) gene expression only:	-	-	-	-	-	-	-
APOBEC2 + APOBEC3B	45.01	53.23	55.81	0.58	0.56	0.56	0.54
IL11, TGFB1, TGFB3	18.86	19.19	19.43	0.57	0.53	0.55	0.55
APOBEC + Cytokines	63.51	71.75	74.84	0.62	0.6	0.6	0.6
Overall survival (OS)							
1) mSMARTcyto	18.46	20.22	20.35	0.58	0.52	0.55	0.56
mSMARTcyto + APOBEC2, APOBEC3B	47.67	53.18	56.15	0.66	0.63	0.64	0.64
mSMARTcyto + IL11, TGFB1, TGFB3	52.42	51.74	54.5	0.66	0.6	0.63	0.65
mSMARTcyto + APOBEC + Cytokines	82.76	82.65	88.22	0.71	0.66	0.69	0.69
2) ISS	75.21	71.09	76.12	0.66	0.54	0.65	0.63
ISS + APOBEC2, APOBEC3B	92.07	94.68	102	0.72	0.65	0.7	0.7
ISS + IL11, TGFB1, TGFB3	77.62	74.89	79.61	0.69	0.63	0.69	0.69
ISS + APOBEC + Cytokines	121.5	125.2	132.8	0.74	0.68	0.73	0.73
3) R-ISS	39.14	39.11	39.23	0.64	0.55	0.61	0.6
R-ISS + APOBEC2, APOBEC3B	64.36	65.24	69.48	0.71	0.62	0.67	0.68
R-ISS + IL11, TGFB1, TGFB3	62.57	60.36	64.59	0.70	0.6	0.68	0.67
R-ISS + APOBEC + Cytokines	93.43	90.28	99.19	0.74	0.66	0.71	0.7
4) R-ISS-nocyto	33.15	32.43	32.63	0.64	0.52	0.63	0.61
R-ISS-nocyto + APOBEC2, APOBEC3B	55.98	58.99	62.18	0.72	0.65	0.69	0.68
R-ISS-nocyto + IL11, TGFB1, TGFB3	57.76	55.47	59.1	0.71	0.65	0.7	0.7
R-ISS-nocyto + APOBEC + Cytokines	83.75	83.38	89.97	0.74	0.68	0.73	0.73
5) blood parameters (β-2-microglobuline, LDH)	58.47	54.58	58.09	0.67	0.64	0.67	0.66
blood parameters* + APOBEC2, APOBEC3B	92.73	93.2	102.6	0.74	0.69	0.72	0.72
blood parameters* + IL11, TGFB1, TGFB3	81.34	78.4	83.48	0.73	0.67	0.72	0.7
blood parameters* + APOBEC + Cytokines (EI-score)	119.3	119.1	130.9	0.76	0.72	0.74	0.75
6) gene expression only:	-	-	-	-	-	-	-
APOBEC2 + APOBEC3B	48.03	53.18	57	0.64	0.54	0.61	0.61
IL11, TGFB1, TGFB3	35.03	36.34	37.99	0.63	0.55	0.61	0.59
APOBEC + Cytokines	85.14	87.42	93.32	0.69	0.64	0.67	0.67