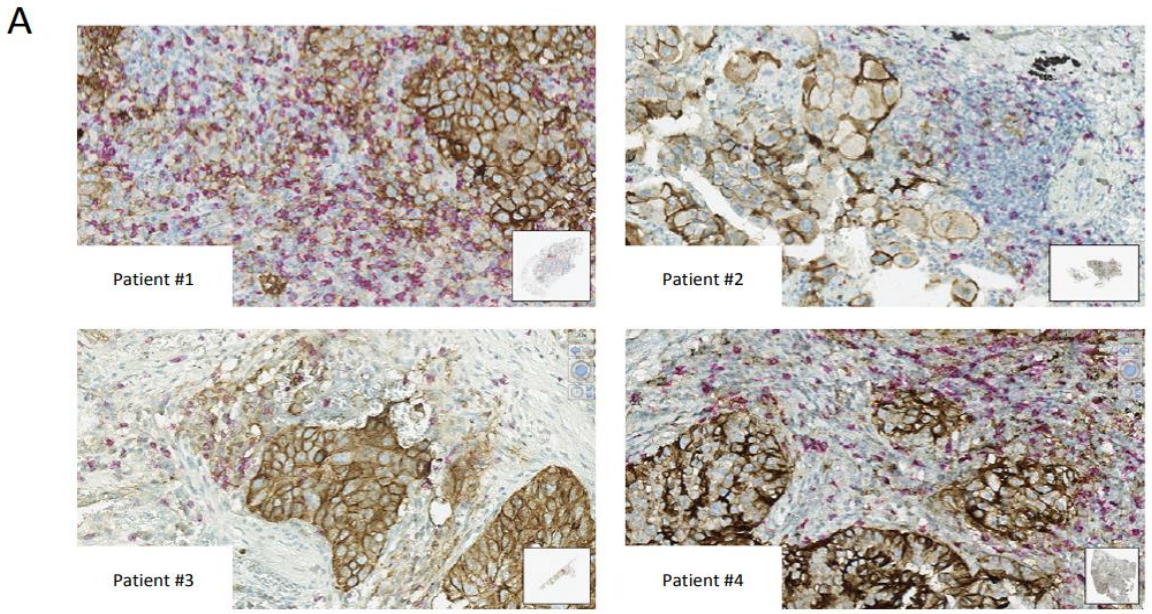
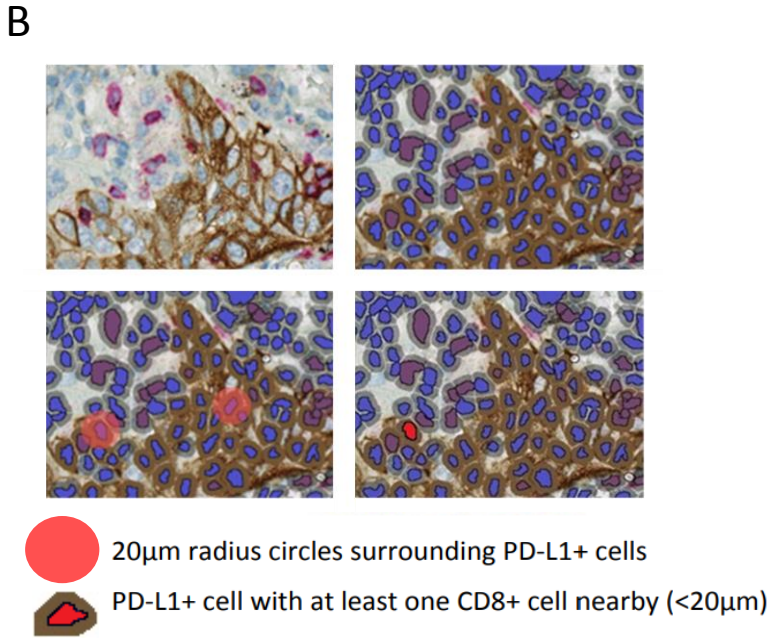

A
Patient #1
Patient #2
Patient #3
Patient #4


B
20µm radius circles surrounding PD-L1+ cells
PD-L1+ cell with at least one CD8+ cell nearby (<20µm)

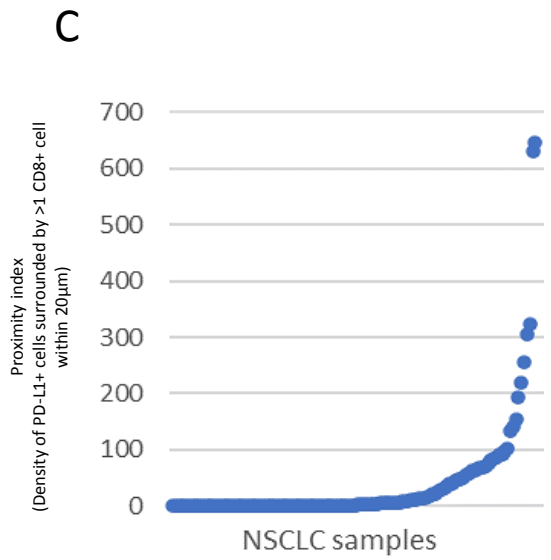

C
Proximity index
(Density of PD-L1+ cells surrounded by >1 CD8+ cell within 20µm)
700
600
500
400
300
200
100
0
NSCLC samples

Figure S1

Training set (Charlie/Delta Cohort)

variables	HR	beta	conf.low	conf.high	p.val	p.val.signif
CD8.Tumor	0.60	-0.51	0.44	0.82	0.00124	**
CD8.Free.TR	0.60	-0.51	0.43	0.82	0.00149	**
CD8.Tumor_nn.20um.clust	0.70	-0.36	0.55	0.88	0.00214	**
CD8.Tumor_nn.20um.prox	0.69	-0.37	0.54	0.88	0.00293	**
PDL1.Tumor_nn.20um.prox	0.70	-0.36	0.55	0.88	0.00303	**
CD8.TSI_nn.20um.prox	0.60	-0.52	0.42	0.86	0.00508	**
PDL1.TSI_nn.20um.prox	0.61	-0.50	0.42	0.87	0.00679	**
PDL1.Tumor_nn.20um.clust	0.81	-0.22	0.68	0.95	0.01140	*
PDL1.TSI_nn.20um.clust	0.76	-0.28	0.59	0.97	0.02550	*
PDL1.TSI	0.77	-0.26	0.61	0.98	0.03480	*
CD8.TSI_nn.20um.clust	0.78	-0.25	0.61	0.99	0.04210	*
PDL1.Tumor	0.85	-0.17	0.72	0.99	0.04270	*
CD8.TSI	0.70	-0.35	0.49	1.00	0.05270	ns
CD8.Free.TSI	0.71	-0.35	0.49	1.02	0.06060	ns
TSI.TR_PDL1.d.ratio	1.05	0.05	0.98	1.12	0.15500	ns
TSI.TR_CD8d.ratio	1.01	0.01	1.00	1.02	0.16300	ns

Univariate Cox Analysis on Continuous Variables (PFS)

variables	HR	beta	conf.low	conf.high	p.val	p.val.signif
CD8.TSI_nn.20um.prox	0.35	-1.10	0.19	0.63	0.00044	***
CD8.Tumor	0.46	-0.78	0.31	0.68	0.00011	***
CD8.Tumor_nn.20um.prox	0.48	-0.73	0.32	0.72	0.00035	***
CD8.Tumor_nn.20um.clust	0.48	-0.73	0.33	0.71	0.00023	***
PDL1.Tumor_nn.20um.prox	0.48	-0.73	0.32	0.72	0.00035	***
PDL1.TSI_nn.20um.prox	0.40	-0.91	0.22	0.72	0.00220	**
PDL1.Tumor	0.56	-0.58	0.38	0.82	0.00270	**
PDL1.Tumor_nn.20um.clust	0.55	-0.59	0.38	0.81	0.00270	**
CD8.Free.TR	0.50	-0.68	0.31	0.81	0.00450	**
TSI.TR_CD8d.ratio	2.40	0.89	1.30	4.60	0.00480	**
CD8.TSI	0.46	-0.77	0.25	0.87	0.01600	*
CD8.Free.TSI	0.48	-0.74	0.26	0.88	0.01800	*
PDL1.TSI	0.55	-0.60	0.33	0.90	0.01700	*
PDL1.TSI_nn.20um.clust	0.56	-0.58	0.34	0.91	0.01900	*
CD8.TSI_nn.20um.clust	0.44	-0.81	0.22	0.90	0.02400	*
TSI.TR_PDL1.d.ratio	1.40	0.36	0.84	2.40	0.19000	ns

Univariate Cox Analysis on Dichotomized Variables (PFS)

Validation set (Mike Cohort)

variables	HR	beta	conf.low	conf.high	p.val	p.val.signif
CD8.Tumor_nn.20um.clust	0.62	-0.47	0.48	0.81	0.000543	***
CD8.Tumor	0.59	-0.53	0.43	0.81	0.000997	***
CD8.Free.TR	0.59	-0.53	0.43	0.81	0.001160	**
CD8.Tumor_nn.20um.prox	0.63	-0.47	0.46	0.85	0.002670	**
PDL1.Tumor_nn.20um.prox	0.64	-0.45	0.47	0.86	0.003070	**
PDL1.Tumor	0.80	-0.22	0.66	0.98	0.027400	*
CD8.TSI_nn.20um.prox	0.68	-0.38	0.48	0.97	0.032500	*
CD8.TSI	0.63	-0.46	0.40	0.99	0.047400	*
PDL1.TSI_nn.20um.prox	0.69	-0.36	0.48	1.00	0.047600	*
CD8.Free.TSI	0.63	-0.46	0.40	1.00	0.050900	ns
PDL1.TSI	0.77	-0.27	0.57	1.02	0.071700	ns
CD8.TSI_nn.20um.clust	0.78	-0.25	0.59	1.05	0.096900	ns
PDL1.Tumor_nn.20um.clust	0.86	-0.16	0.70	1.04	0.117000	ns
TSI.TR_PDL1.d.ratio	1.02	0.02	0.98	1.07	0.282000	ns
TSI.TR_CD8d.ratio	1.08	0.07	0.93	1.24	0.316000	ns
PDL1.TSI_nn.20um.clust	0.88	-0.13	0.68	1.14	0.332000	ns

Univariate Cox Analysis on Continuous Variables (PFS)

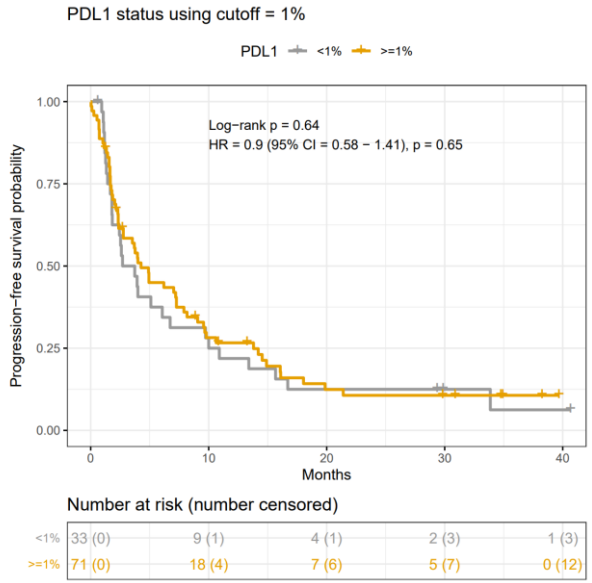
variables	HR	beta	conf.low	conf.high	p.val	p.val.signif
CD8.Tumor_nn.20um.clust	0.41	-0.88	0.28	0.62	1.6e-05	****
CD8.Tumor	0.42	-0.86	0.28	0.64	5.3e-05	****
PDL1.Tumor_nn.20um.prox	0.40	-0.91	0.26	0.63	7.2e-05	****
CD8.Tumor_nn.20um.prox	0.44	-0.81	0.29	0.68	2.1e-04	***
CD8.Free.TR	0.44	-0.82	0.28	0.69	3.8e-04	***
CD8.TSI_nn.20um.prox	0.38	-0.98	0.21	0.68	1.2e-03	**
PDL1.TSI_nn.20um.prox	0.38	-0.96	0.21	0.69	1.6e-03	**
CD8.TSI	0.25	-1.40	0.09	0.70	8.4e-03	**
CD8.Free.TSI	0.25	-1.40	0.09	0.70	8.4e-03	**
TSI.TR_PDL1.d.ratio	2.20	0.80	1.20	4.10	1.2e-02	*
CD8.TSI_nn.20um.clust	0.30	-1.20	0.11	0.82	2.0e-02	*
PDL1.Tumor_nn.20um.clust	0.59	-0.53	0.39	0.90	1.4e-02	*
PDL1.TSI	0.49	-0.72	0.27	0.89	1.9e-02	*
PDL1.Tumor	0.59	-0.53	0.38	0.92	2.0e-02	*
PDL1.TSI_nn.20um.clust	0.49	-0.71	0.26	0.92	2.6e-02	*
TSI.TR_CD8d.ratio	1.50	0.40	0.91	2.40	1.2e-01	ns

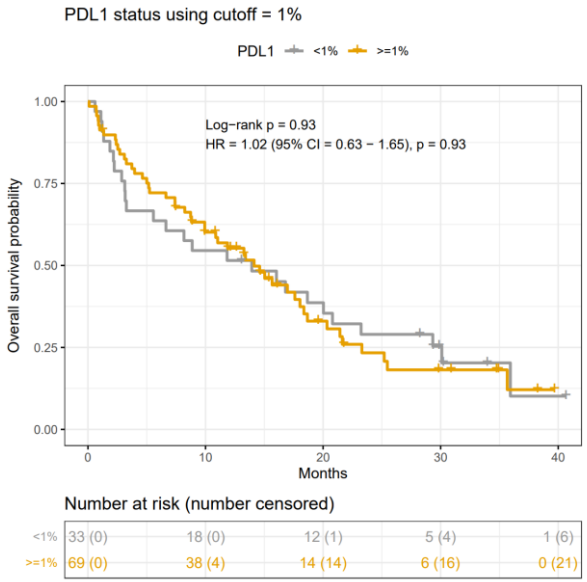
Univariate Cox Analysis on Dichotomized Variables (PFS)

Figure S2

Training set (Charlie/Delta Cohort)

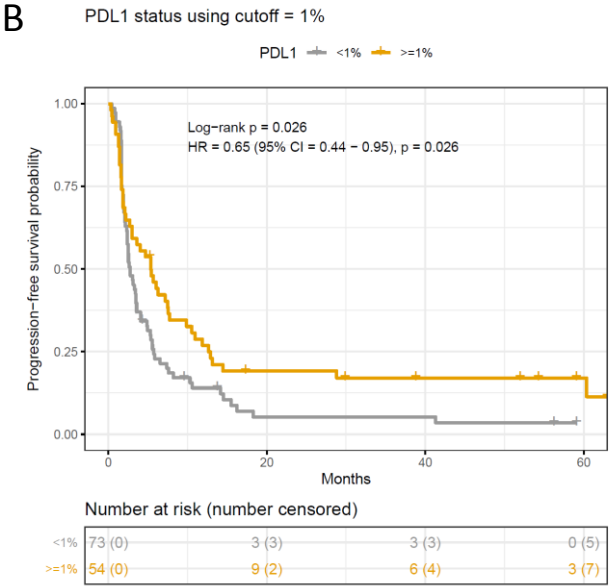
A





Validation set (Mike Cohort)

B



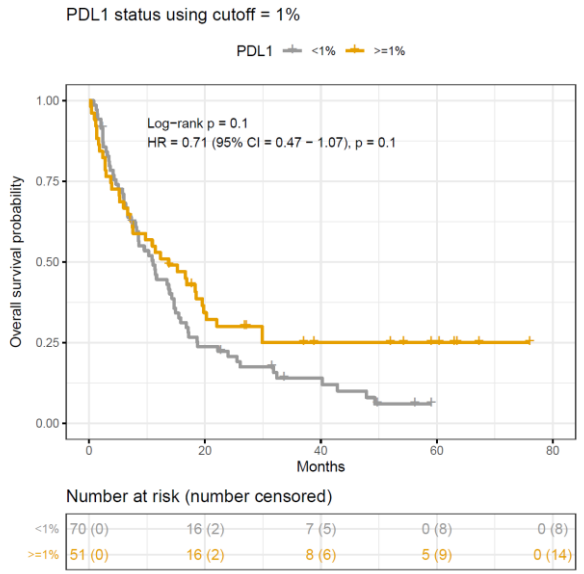
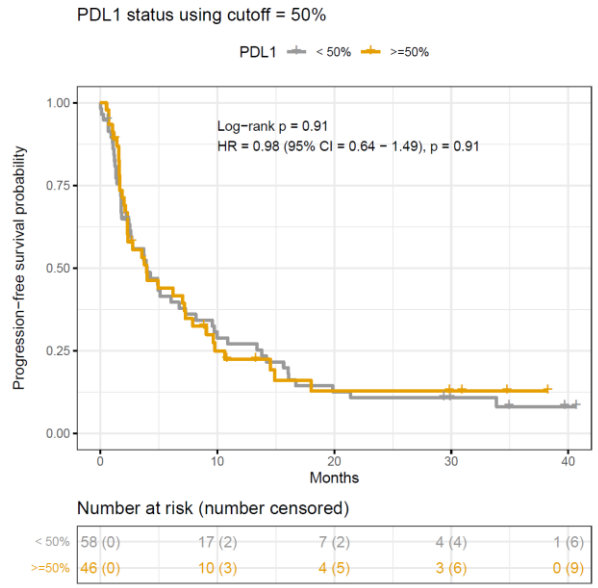
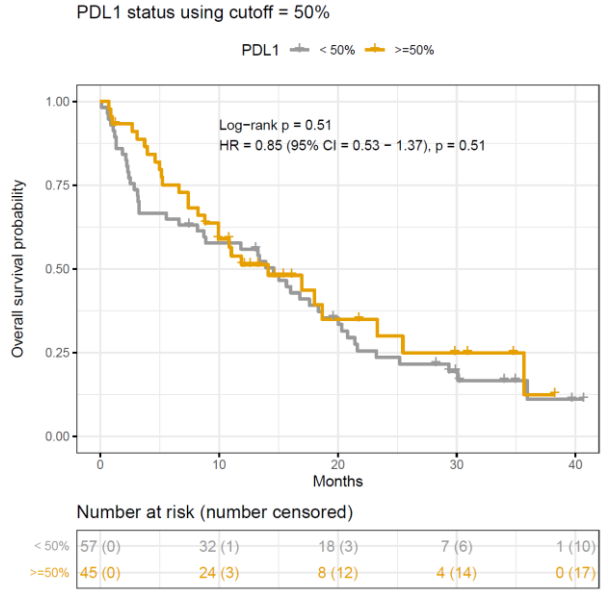


Figure S3

Training set (Charlie/Delta Cohort)

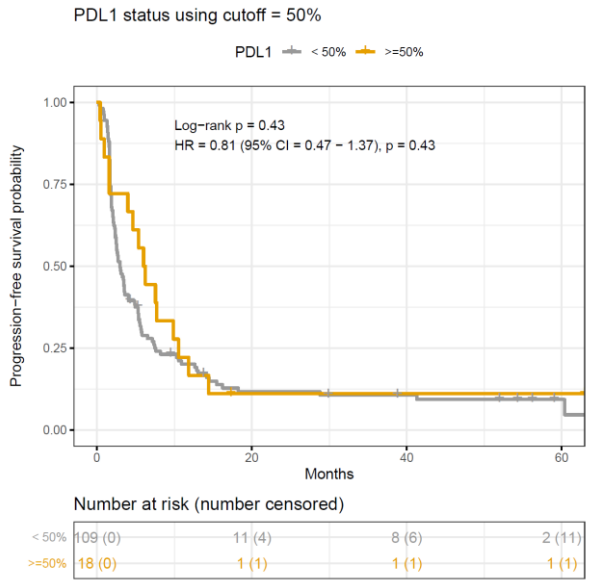
C





Validation set (Mike Cohort)

D



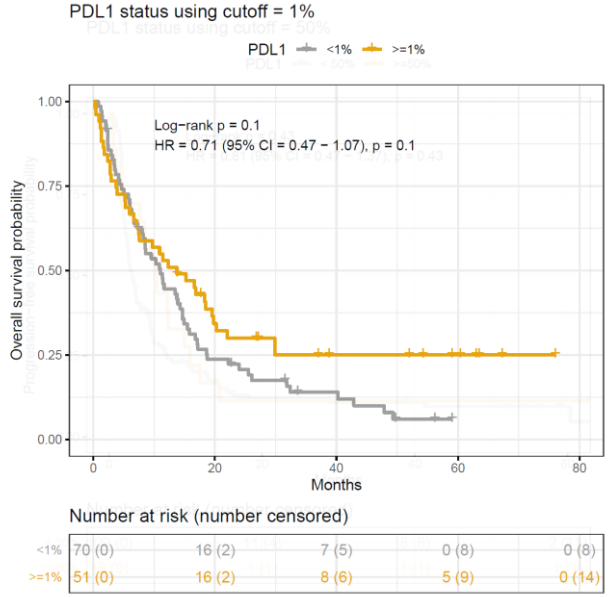
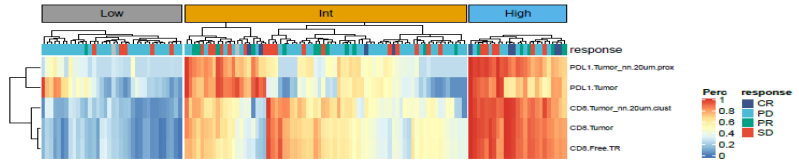


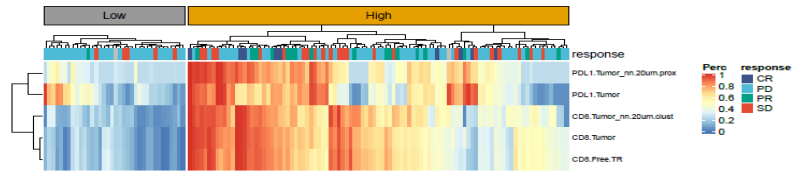
Figure S3

Training set (Charlie/Delta Cohort)

A **Immunoscore IC (Three groups)**

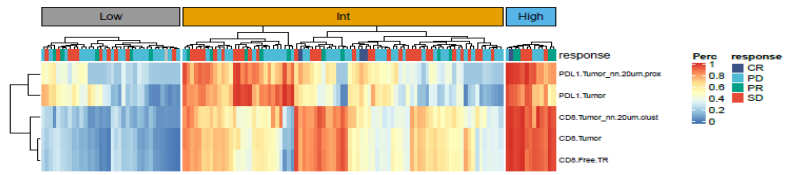


B **Immunoscore IC (Two groups)**



Validation set (Mike Cohort)

C **Immunoscore IC (Three groups)**



D **Immunoscore IC (Two groups)**

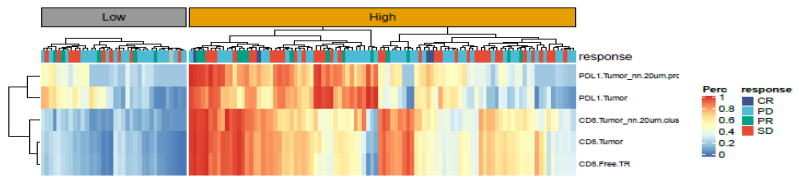


Figure S4

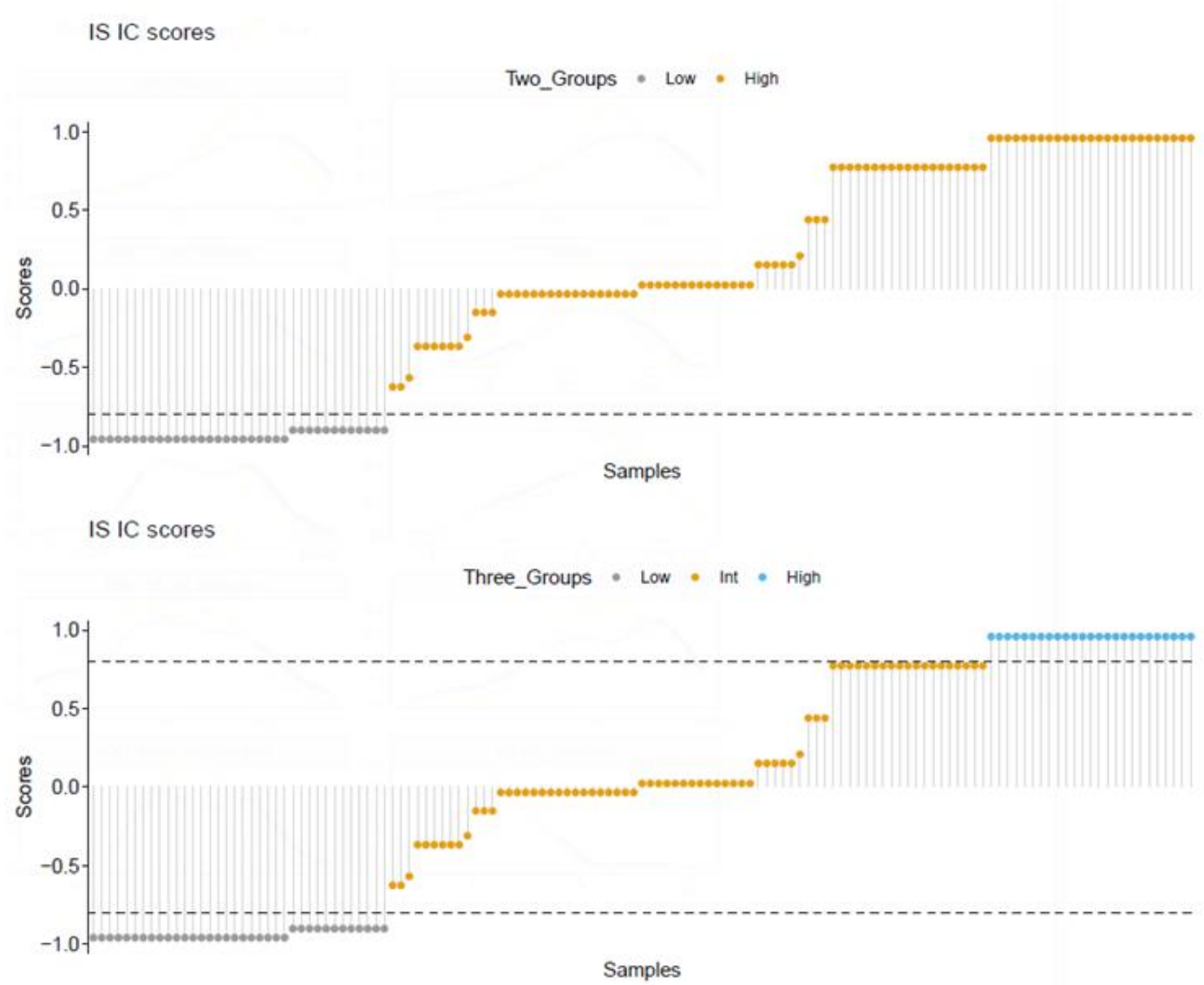

IS IC scores
Two_Groups
Low
High
1.0
0.5
0.0
−0.5
−1.0
Scores
Samples
IS IC scores
Three_Groups
Low
Int
High
1.0
0.5
0.0
−0.5
−1.0
Scores
Samples

Figure S5

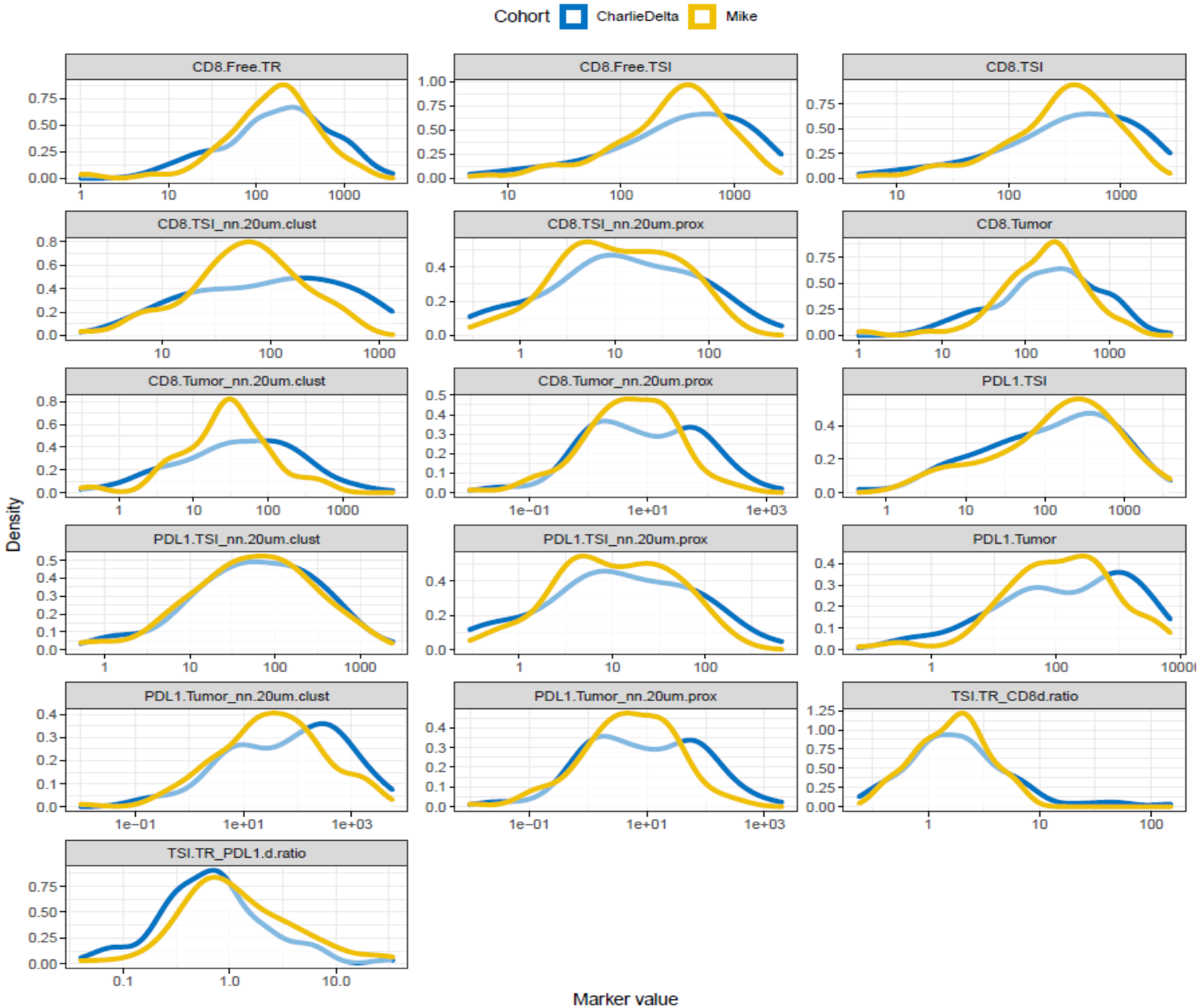

Cohort
CharlieDelta
Mike
CD8.Free.TR
CD8.Free.TSI
CD8.TSI
CD8.TSI_nn.20um.clust
CD8.TSI_nn.20um.prox
CD8.Tumor
CD8.Tumor_nn.20um.clust
CD8.Tumor_nn.20um.prox
PDL1.TSI
PDL1.TSI_nn.20um.clust
PDL1.TSI_nn.20um.prox
PDL1.Tumor
PDL1.Tumor_nn.20um.clust
PDL1.Tumor_nn.20um.prox
TSI.TR_CD8d.ratio
TSI.TR_PDL1.d.ratio
Density
Marker value

Figure S6