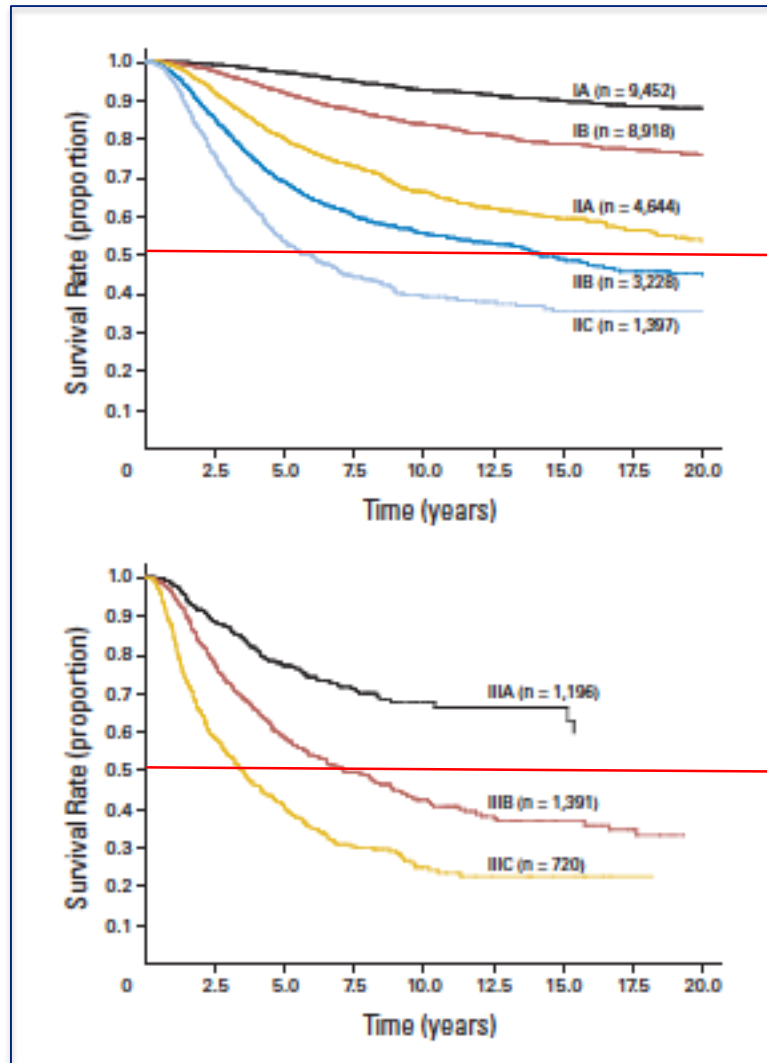




Combining transcriptomic and tissue-based biomarkers to improve recurrence prediction in stage II-III melanoma

SITC Oral Abstract Presentation
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Division of Pediatric Hematology/Oncology

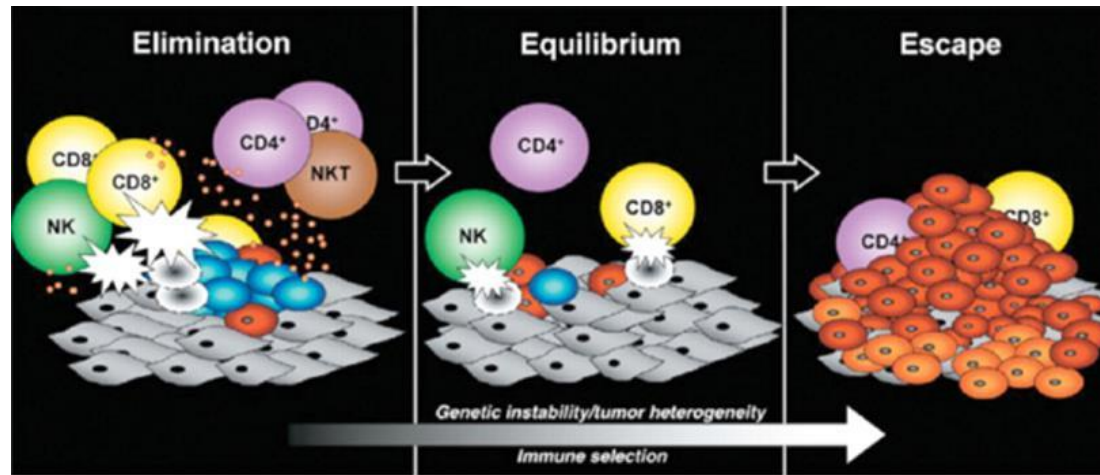
Stage II-III Melanoma



- High degree of heterogeneity among patients within the same stage
 - Variable survival ranging 25-55%
- Overlapping survival among stage II-III
 - Stage IIB and C worse than IIIA



Who should we treat with immunotherapy?



- Immunotherapy can be effective after surgery in preventing recurrence
- Treat all patients?
 - High toxicity
 - High cost (\$20,000 / mo)
- Treat only recurrent patients?





Prognostic tools to stratify Stage II-III melanoma patients

Genomic Signature Melanoma Immune Profile (MIP)

Precision Medicine and Imaging

Validation of Melanoma Immune Profile (MIP), a Prognostic Immune Gene Prediction Score for Stage II-III Melanoma

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Shumin Rui⁴, Marc S. Ernstoff⁵, Bret Taback¹, Sarabjot Pabla⁶, Rui Chang⁷, Sandra J. Lee⁸,
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Clinical
Cancer
Research



Research Article

Quantitative Analysis of Immune Infiltrates in Primary Melanoma

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Danielle R. Davari³, Alan Wu⁵, Zoë Blake², Yan Lu², Kayleigh N. Askin³,
Anthea Monod⁶, Camden L. Esancy², Edward C. Stack⁷, Dan Tong Jia⁸,
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Howard L. Kaufman¹⁰, Charles G. Drake², Basil A. Horst¹¹, and Yvonne M. Saenger²

Cancer
Immunology
Research

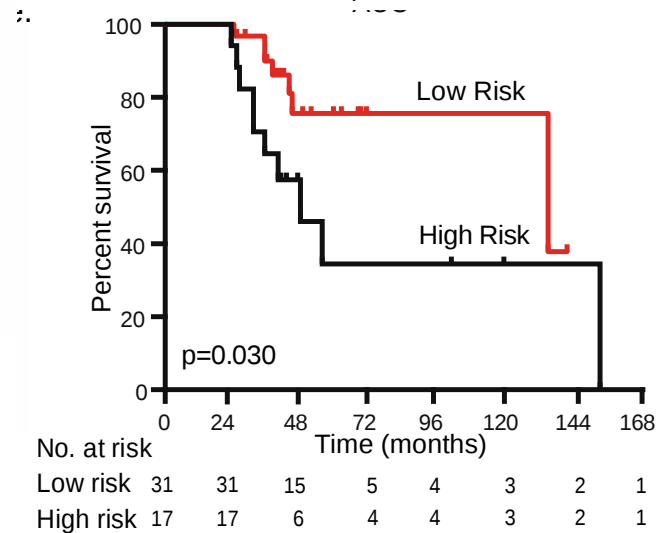
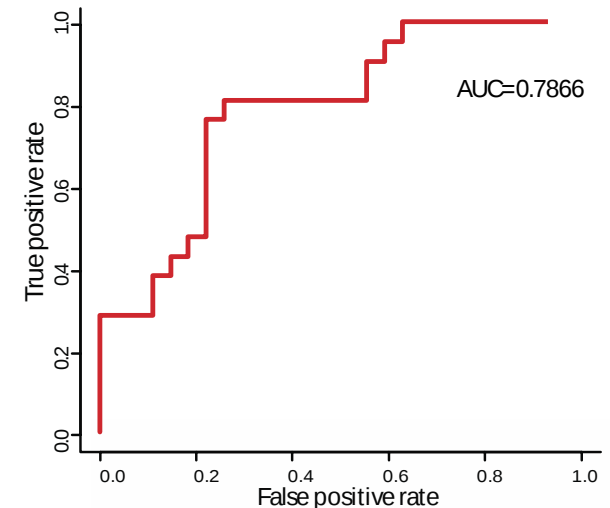
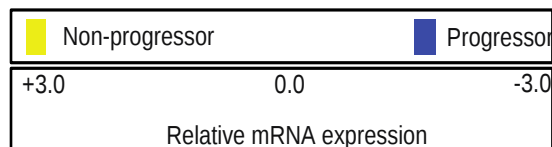
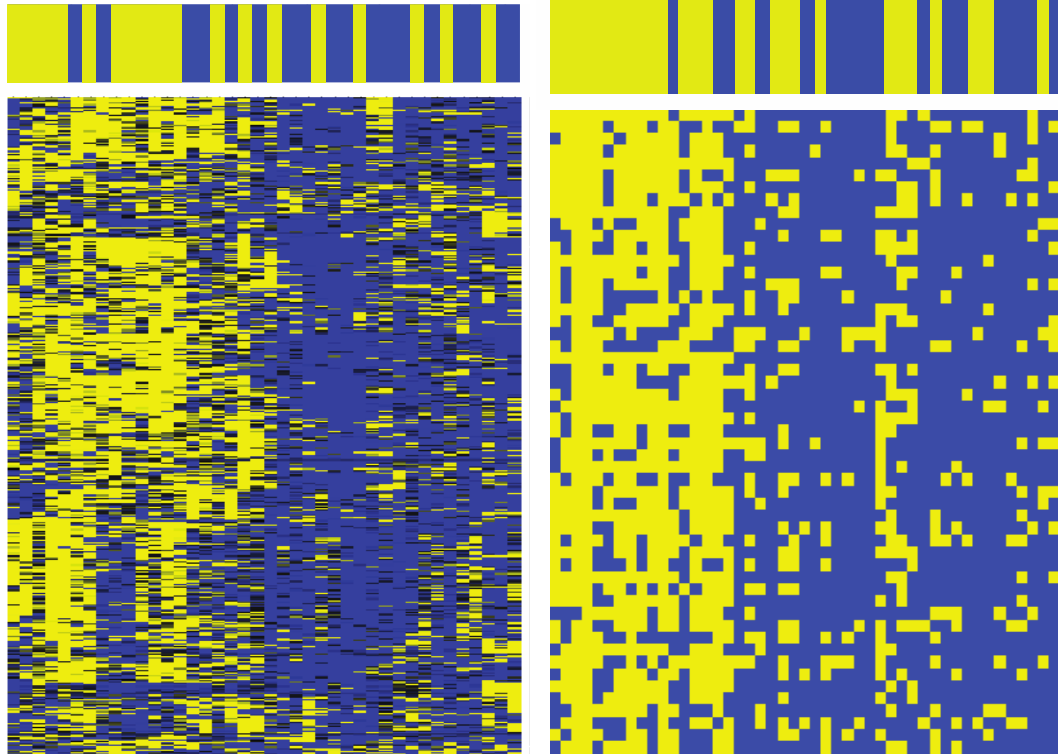


CD8/CD68
ratio

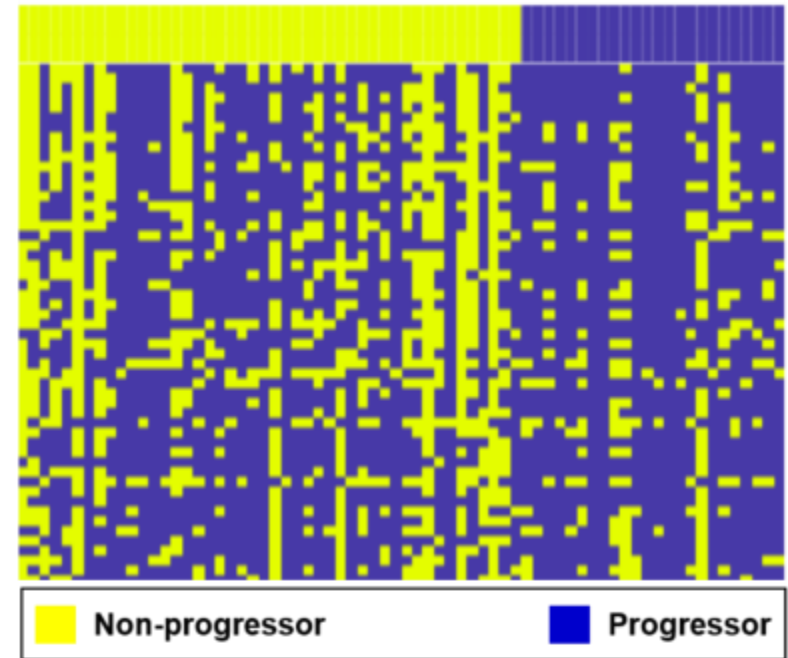
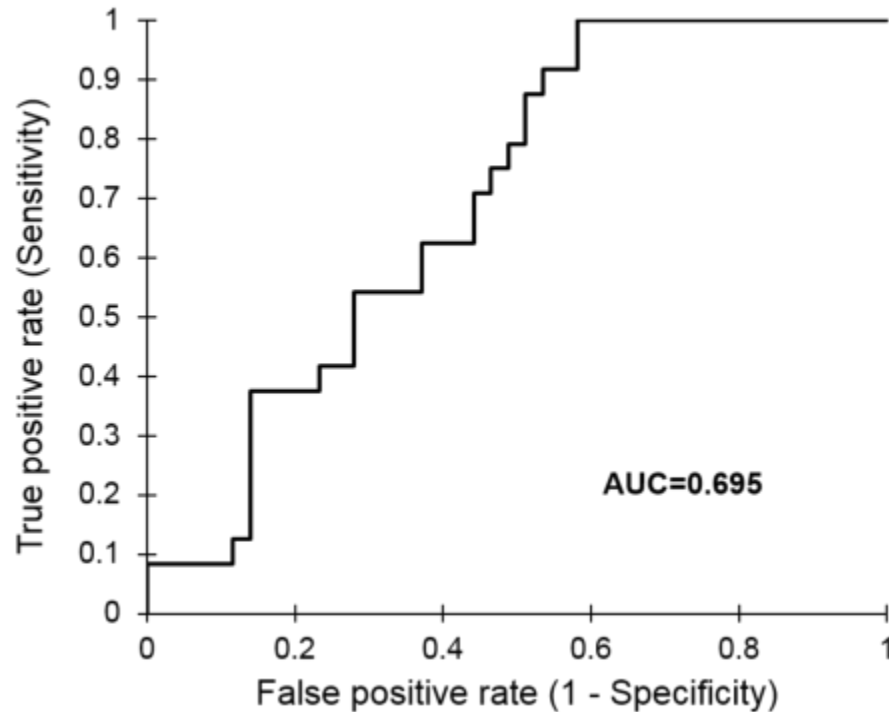
Melanoma Immune Profile (MIP)

Training Set

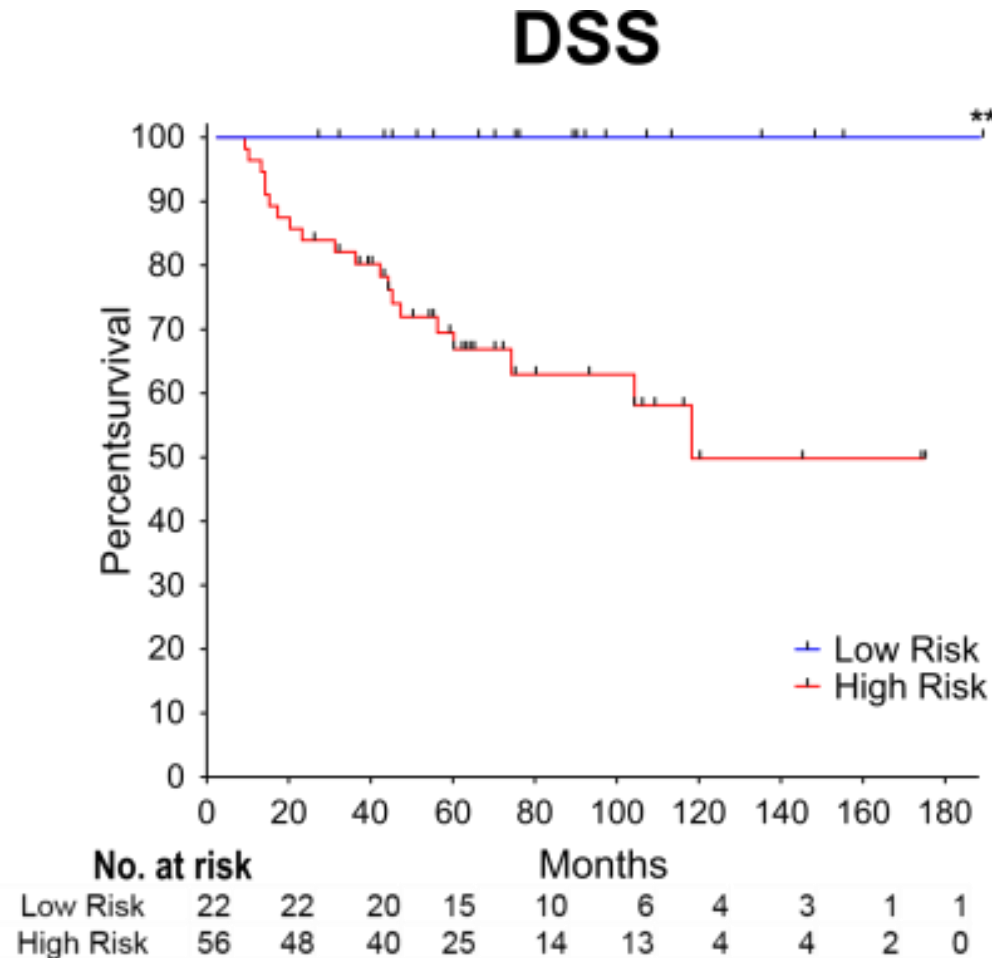
Test Set



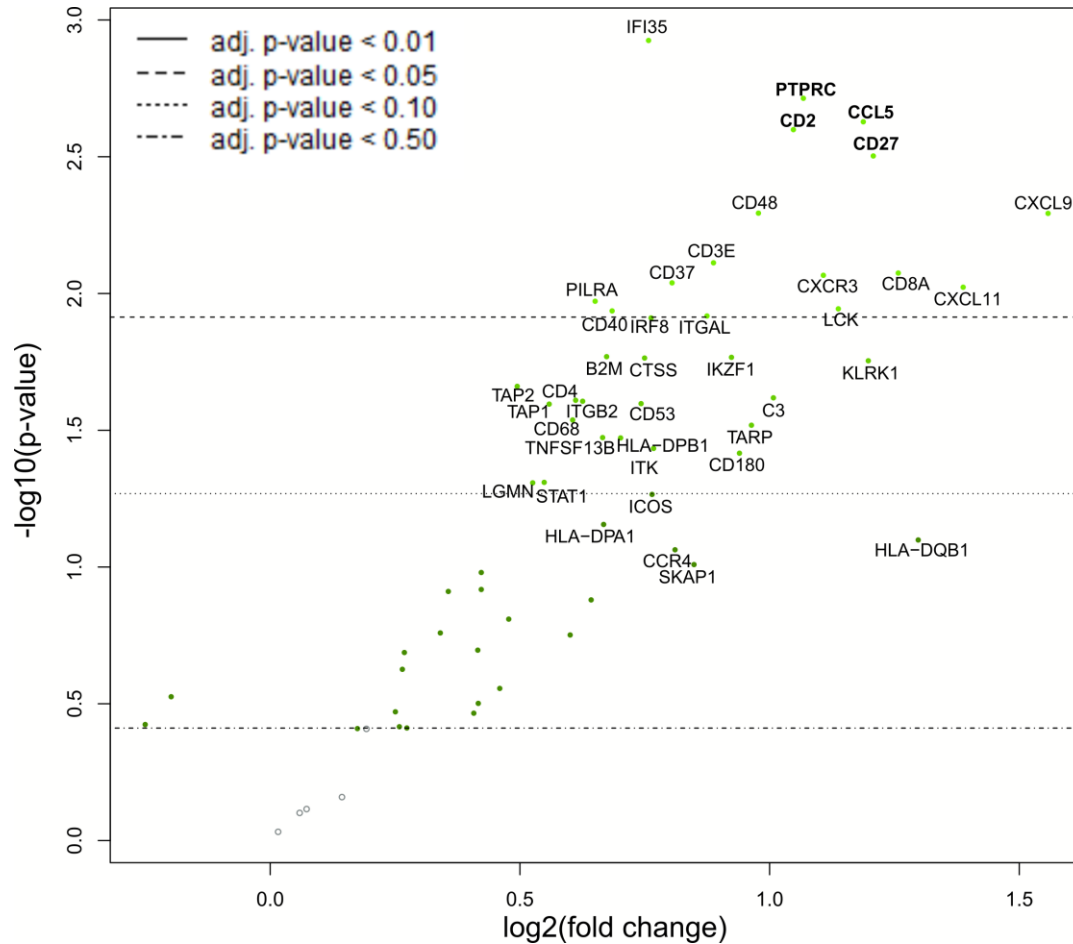
MIP further validated using 78 CUIMC patients



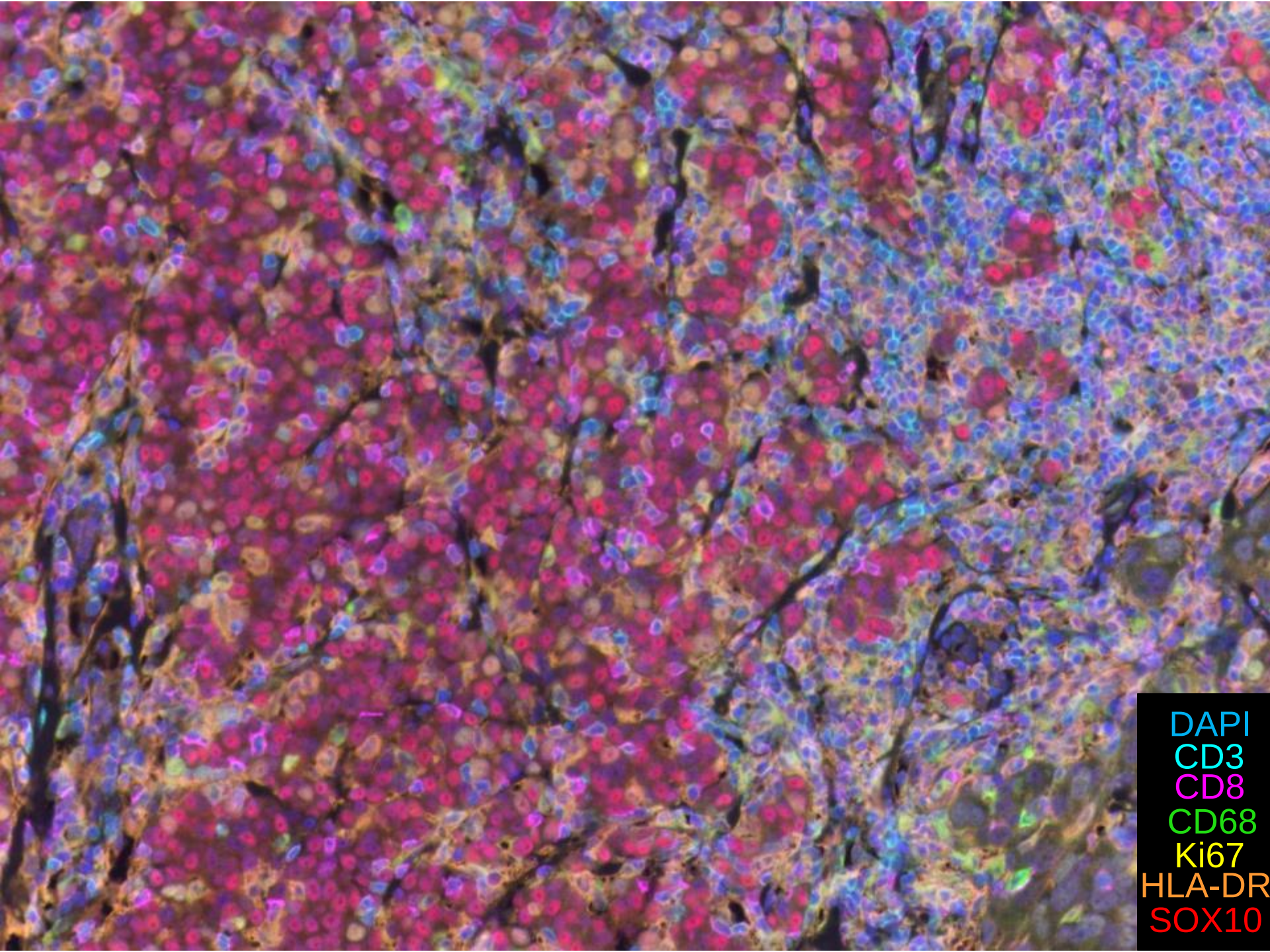
MIP correlates with disease specific survival



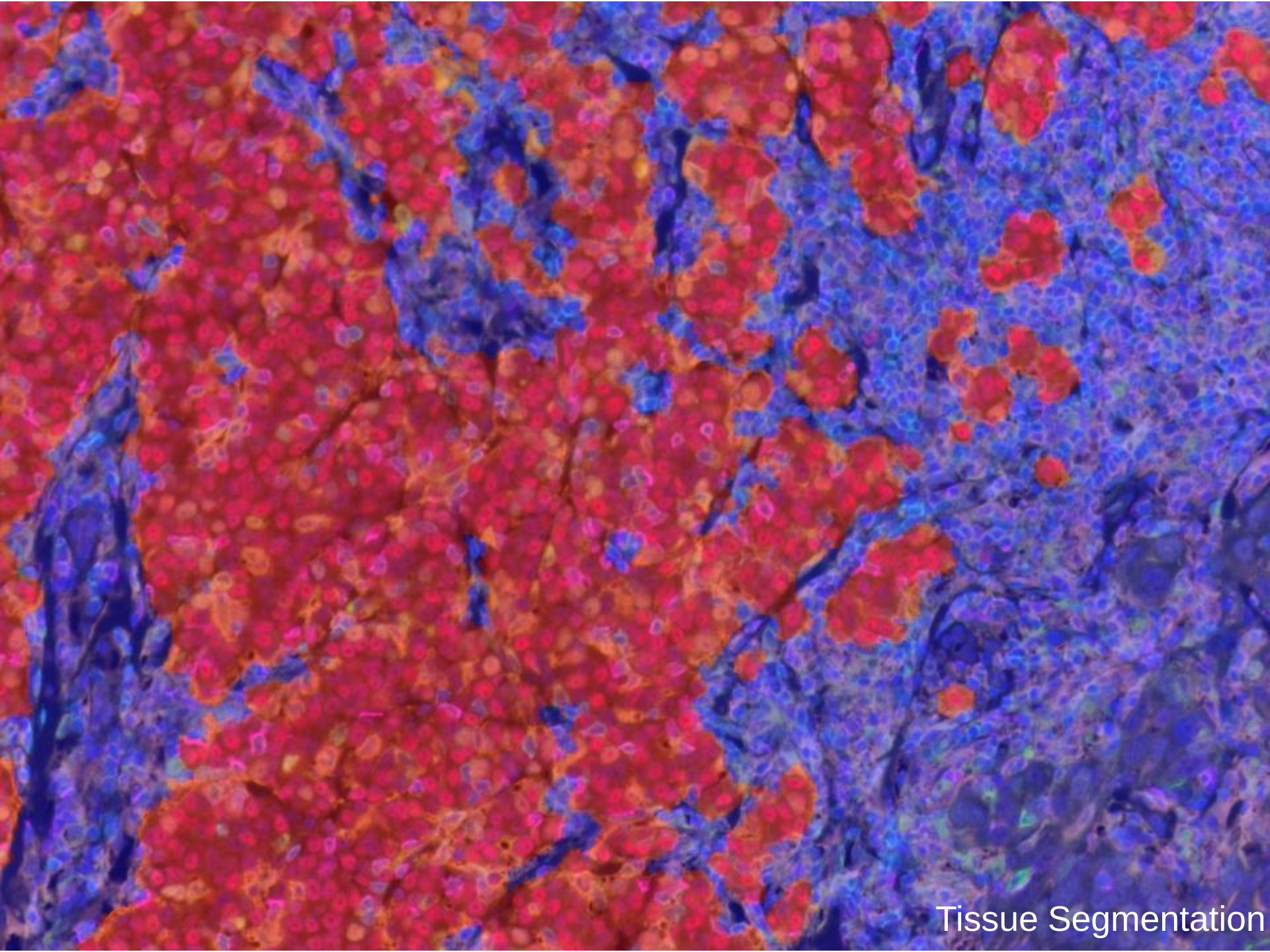
Top Genes in MIP differentiate non-recurrent patients from recurrent



Gene	Differential expression	
	Fold Change	BH p value
<i>PTPRC</i>	1.07	0.0399
<i>CCL5</i>	1.19	0.0399
<i>CD2</i>	1.05	0.0399
<i>CD27</i>	1.21	0.04
<i>CXCL9</i>	1.56	0.0459
<i>CD8A</i>	1.26	0.0459
<i>CXCR3</i>	1.11	0.0459
<i>CXCL11</i>	1.39	0.0459
<i>LCK</i>	1.14	0.0459

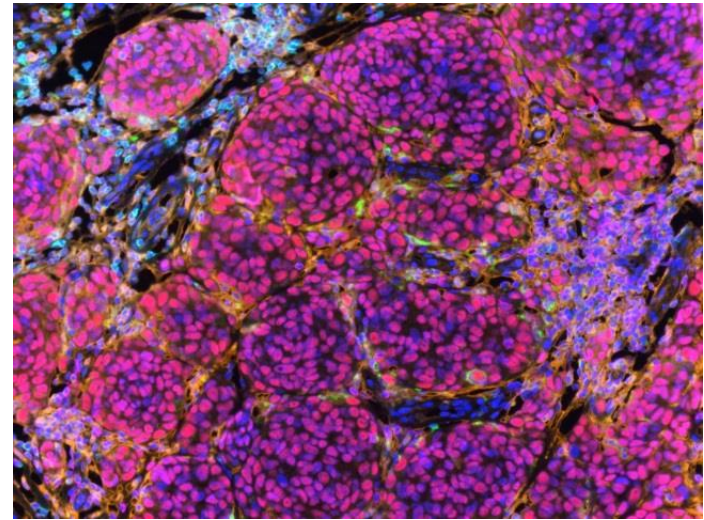
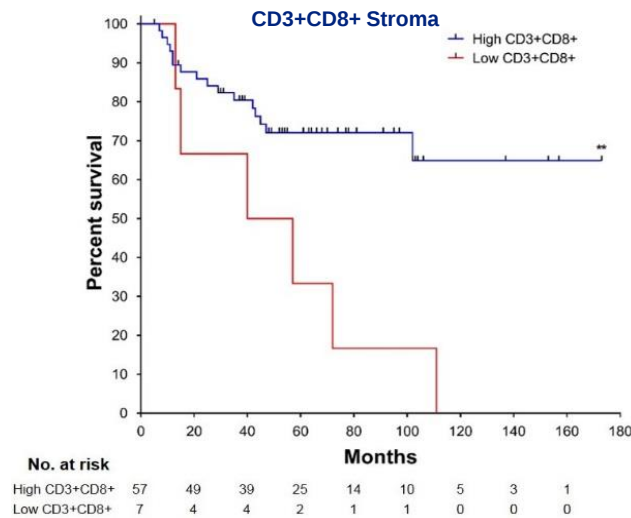
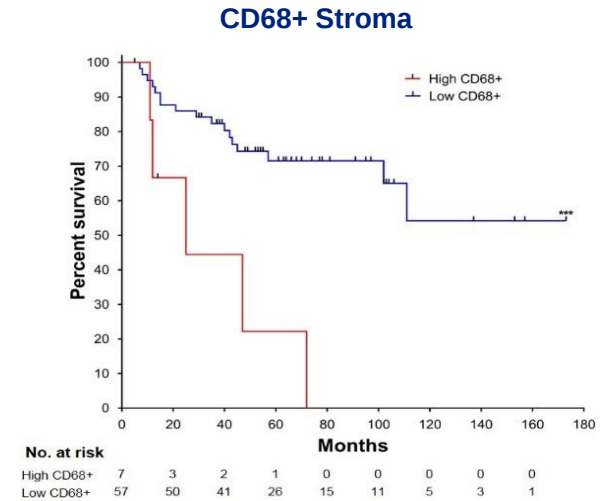
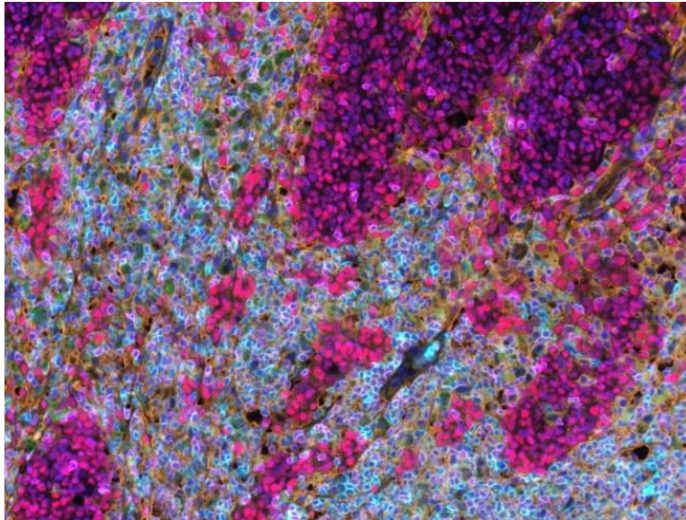


DAPI
CD3
CD8
CD68
Ki67
HLA-DR
SOX10

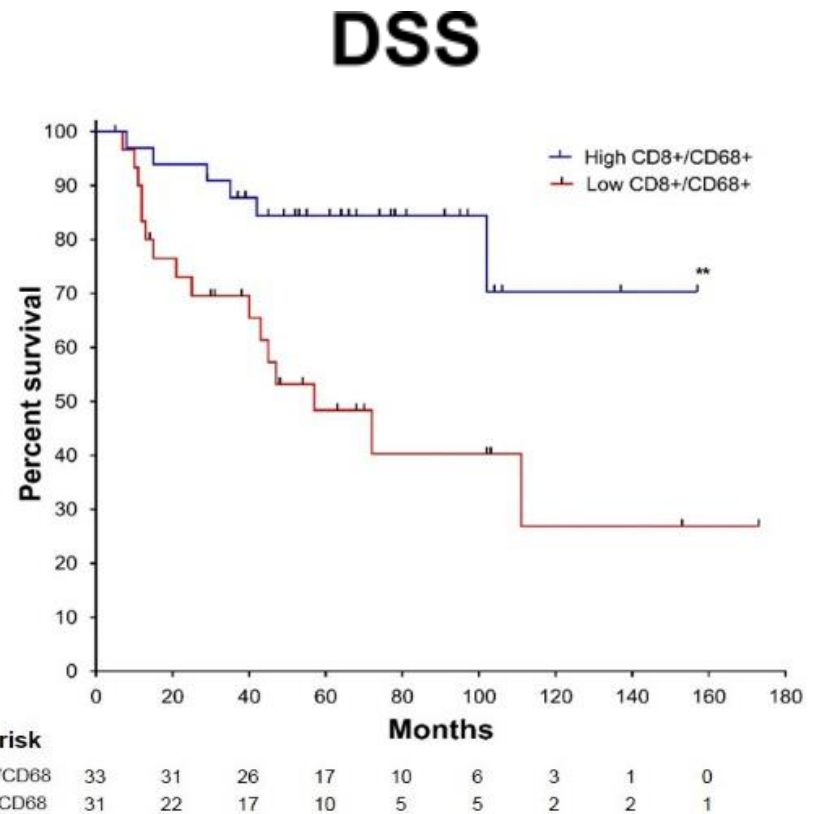
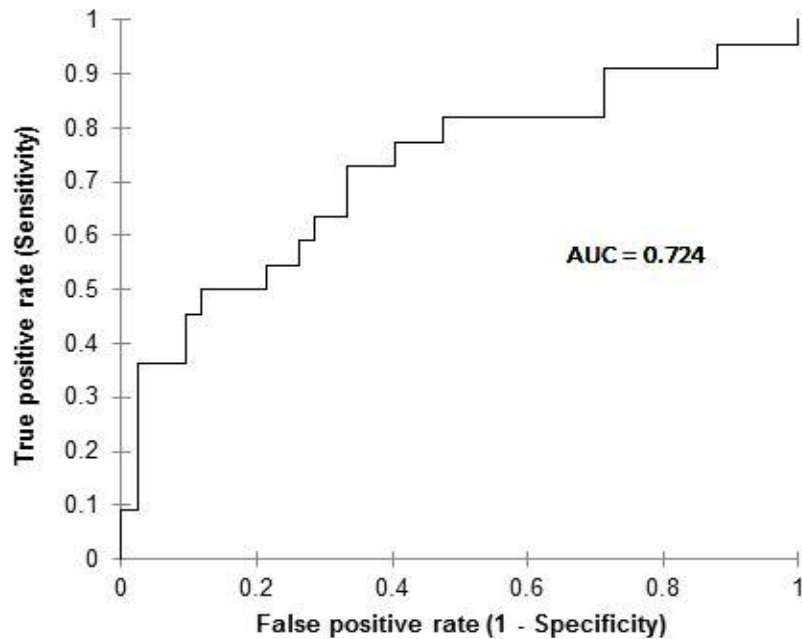


Tissue Segmentation

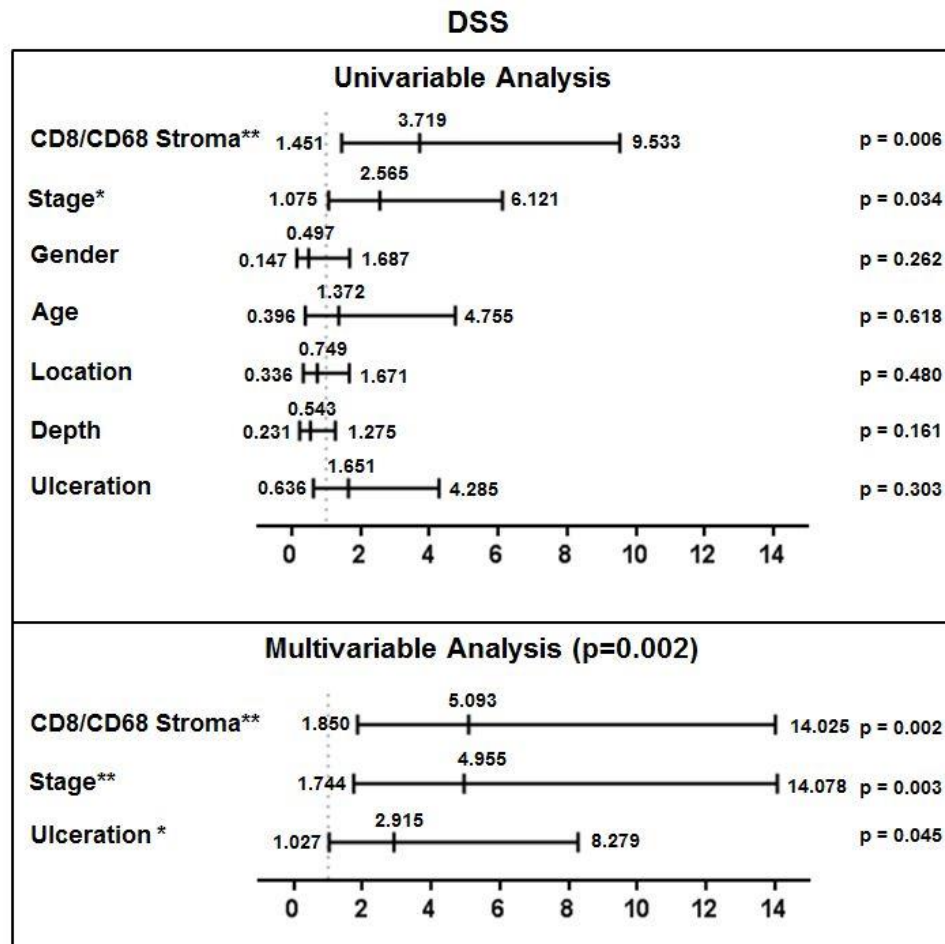
CD8+ and CD68+ cells in stroma correlate with DSS



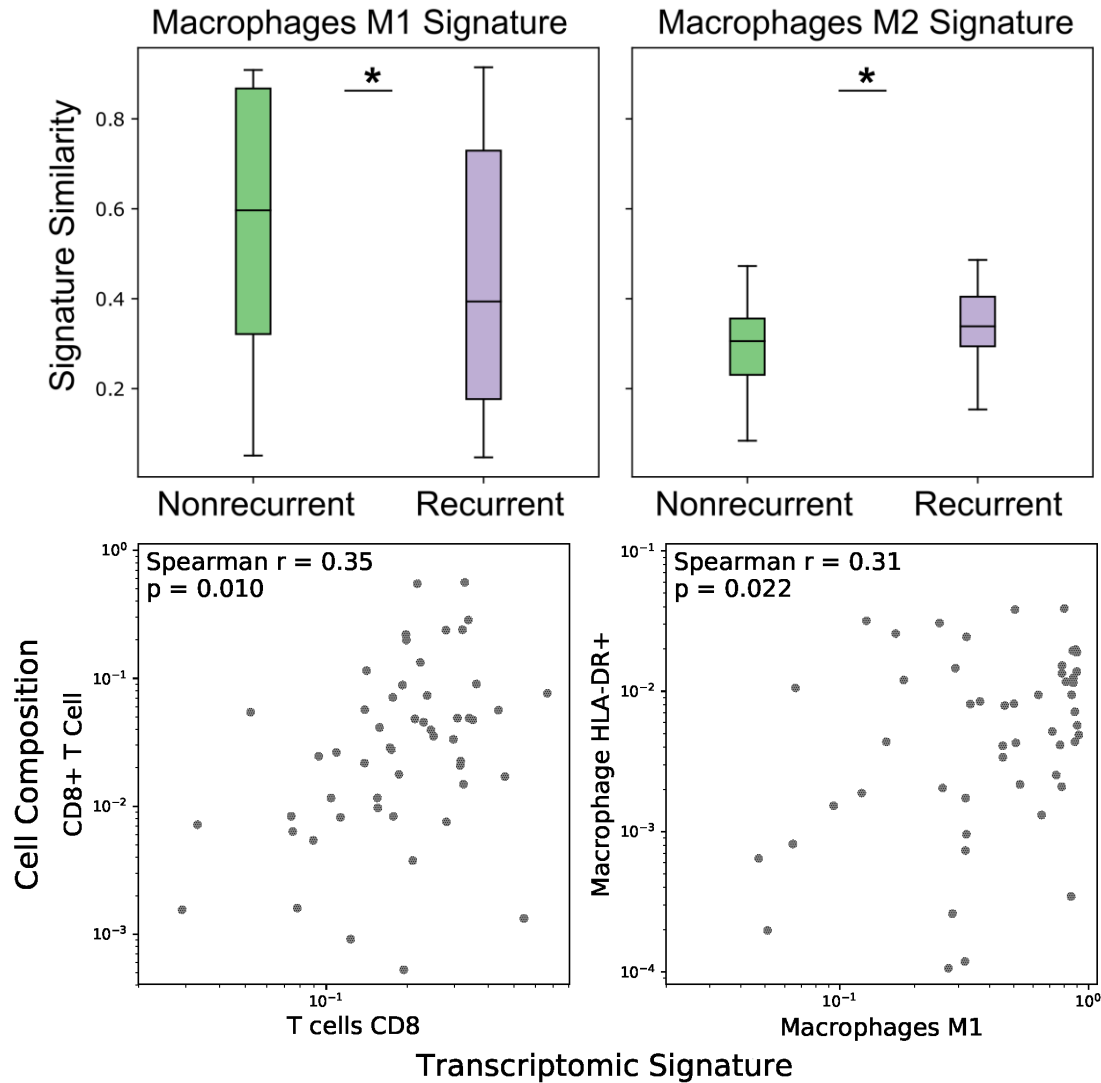
High CD8/CD68 Ratio predicts good DSS



Ratio of CD8+/CD68+ as Biomarker



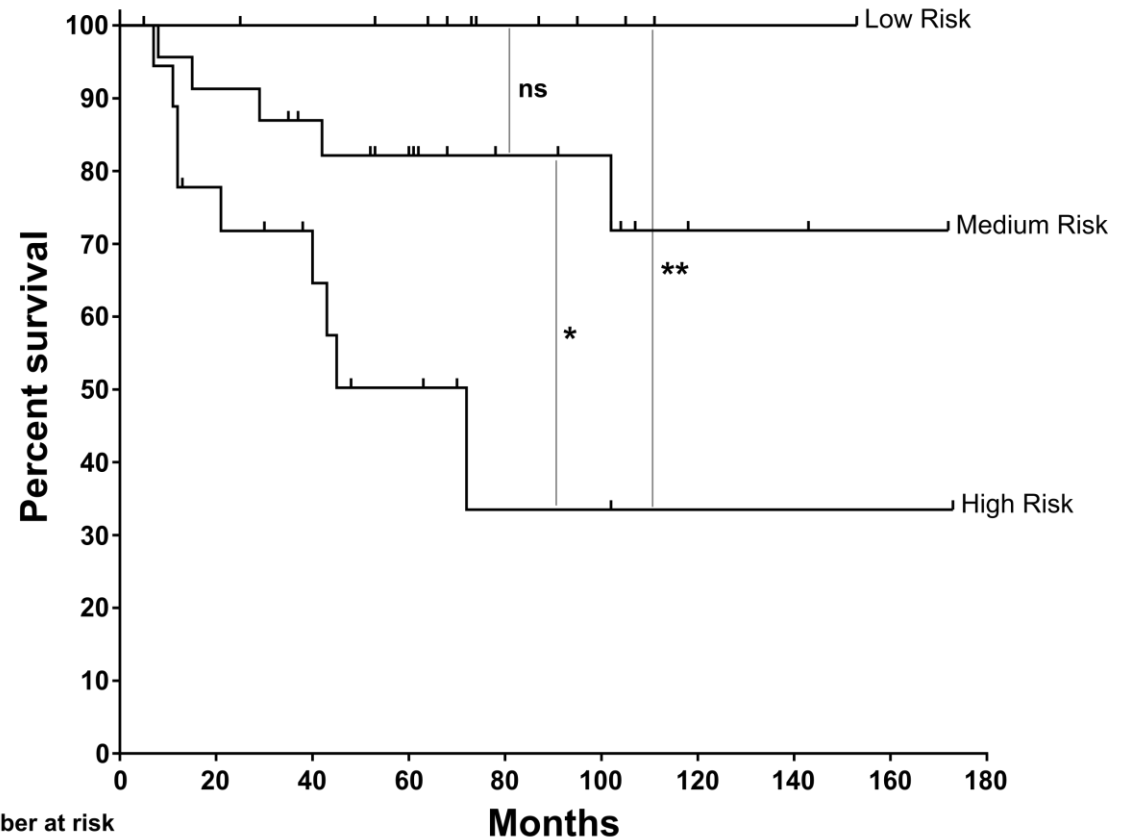
Linking MIP and multiplex IF



MIP + CD8/CD68 ratio defines risk groups

DSS: MIP and CD8/CD68 ratio

Gene	CD8/CD68 Stroma
<i>PTPRC</i>	0.05
<i>CCL5</i>	0.21
<i>CD2</i>	0.07
<i>CD27</i>	0.04
<i>CXCL9</i>	0.19
<i>CD8A</i>	0.16
<i>CXCR3</i>	0.19
<i>CXCL11</i>	0.2
<i>LCK</i>	-0.03



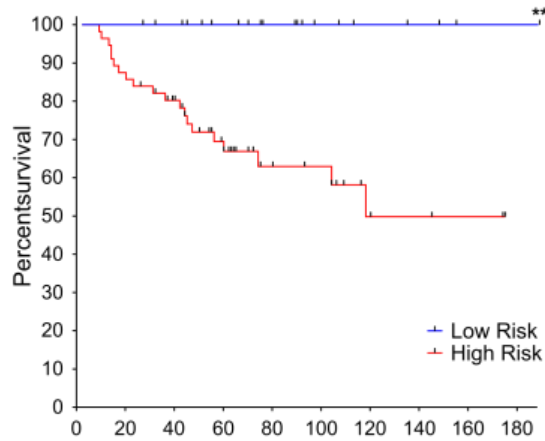
Number at risk

	0	20	40	60	80	100	120	140	160	180
Low Risk	11	11	10	9	5	3	1	1	0	0
Medium Risk	23	21	18	15	9	8	3	3	1	0
High Risk	19	13	10	6	2	2	1	1	1	0



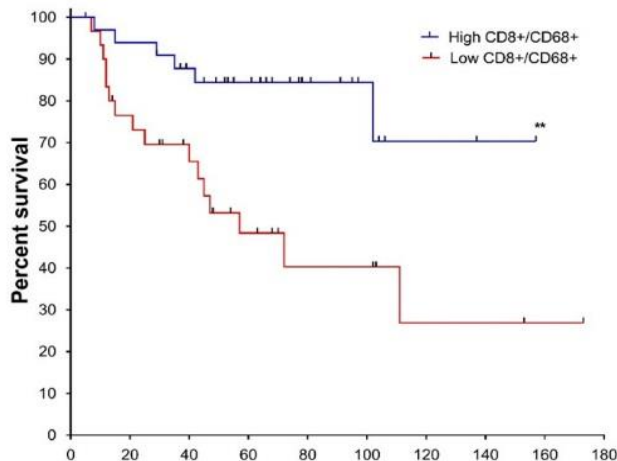
MIP + CD8/CD68 ratio defines risk groups

MIP



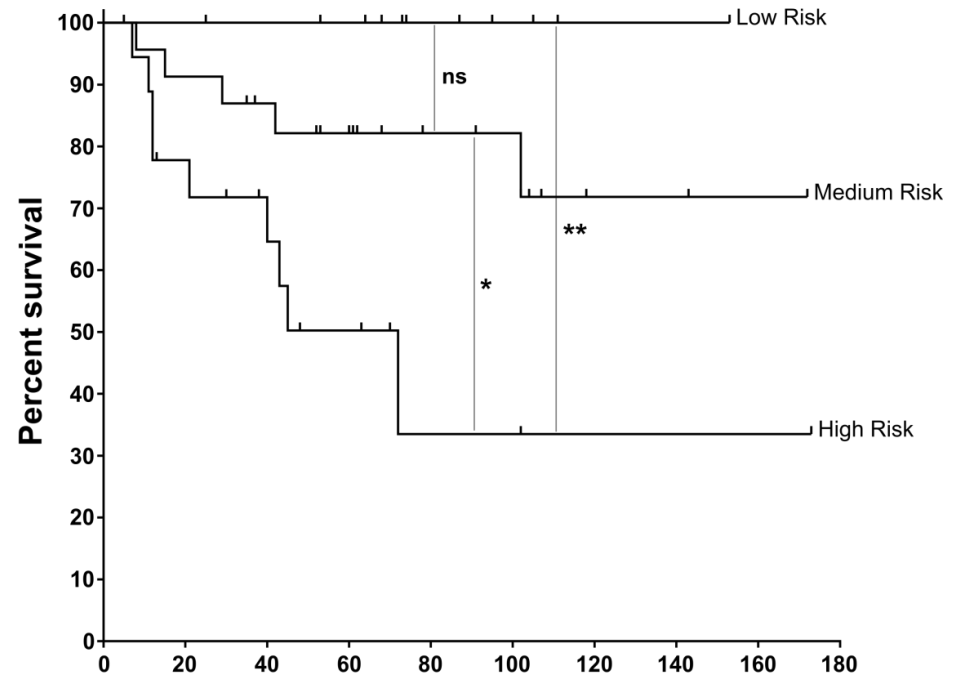
No. at risk	Months									
Low Risk	22	22	20	15	10	6	4	3	1	1
High Risk	56	48	40	25	14	13	4	4	2	0

CD8/CD68 Ratio



No. at risk	Months									
High CD8/CD68	33	31	26	17	10	6	3	1	0	
Low CD8/CD68	31	22	17	10	5	5	2	2	1	

DSS: MIP and CD8/CD68 ratio



Number at risk	Months									
Low Risk	11	11	10	9	5	3	1	1	0	0
Medium Risk	23	21	18	15	9	8	3	3	1	0
High Risk	19	13	10	6	2	2	1	1	1	0



Acknowledgements

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Questions?