

Analysis of H&E Images Using Deep Learning for the Prediction of Distant Metastatic Recurrence in Early Stage Melanoma

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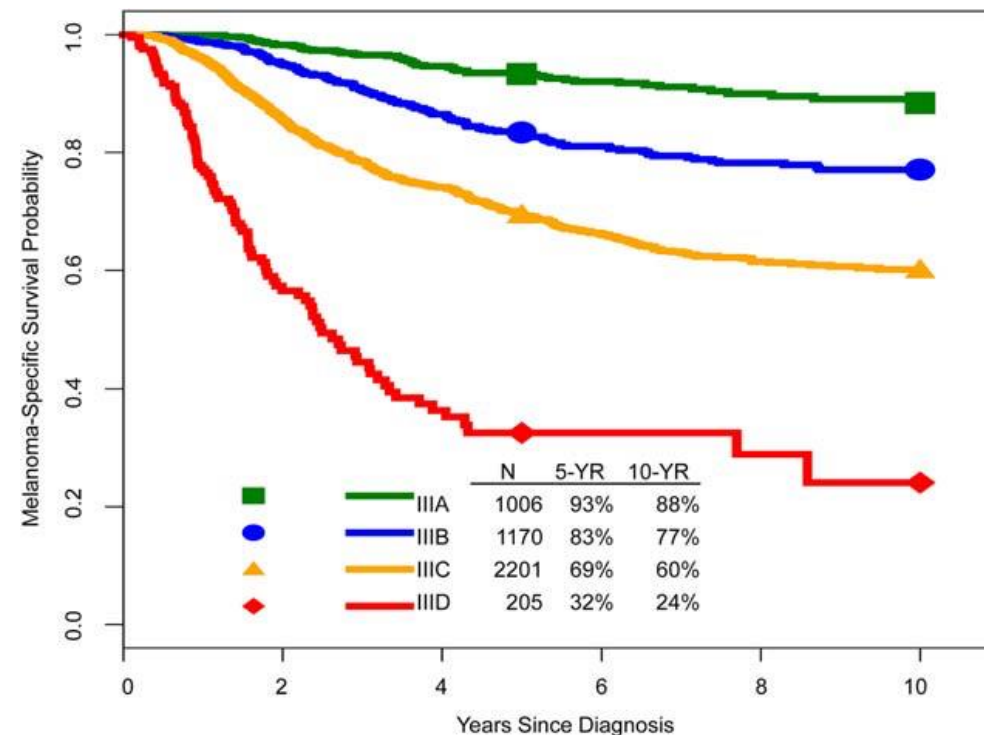
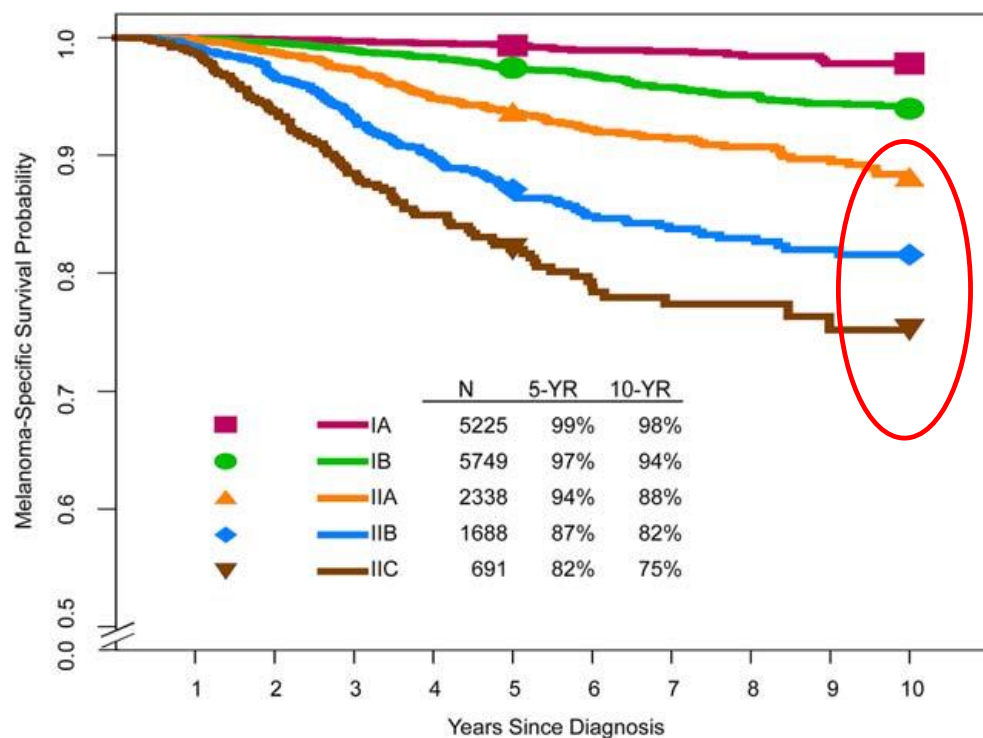
SITC Annual Meeting

November 8, 2019

Disclosures

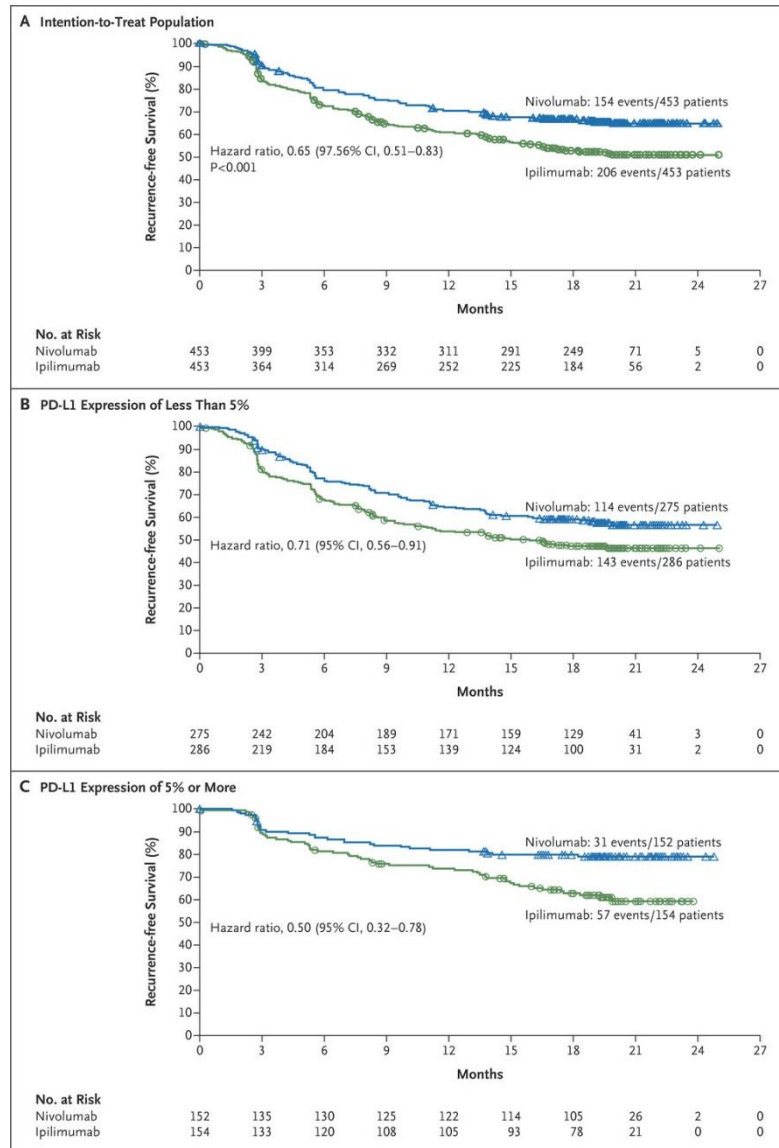
- Co-founder of Wasaba, a company with a focus on artificial intelligence based digital pathology biomarkers.
- Research funding from Amgen and Regeneron

Melanoma Staging is Critical but Imprecise...and Confusing



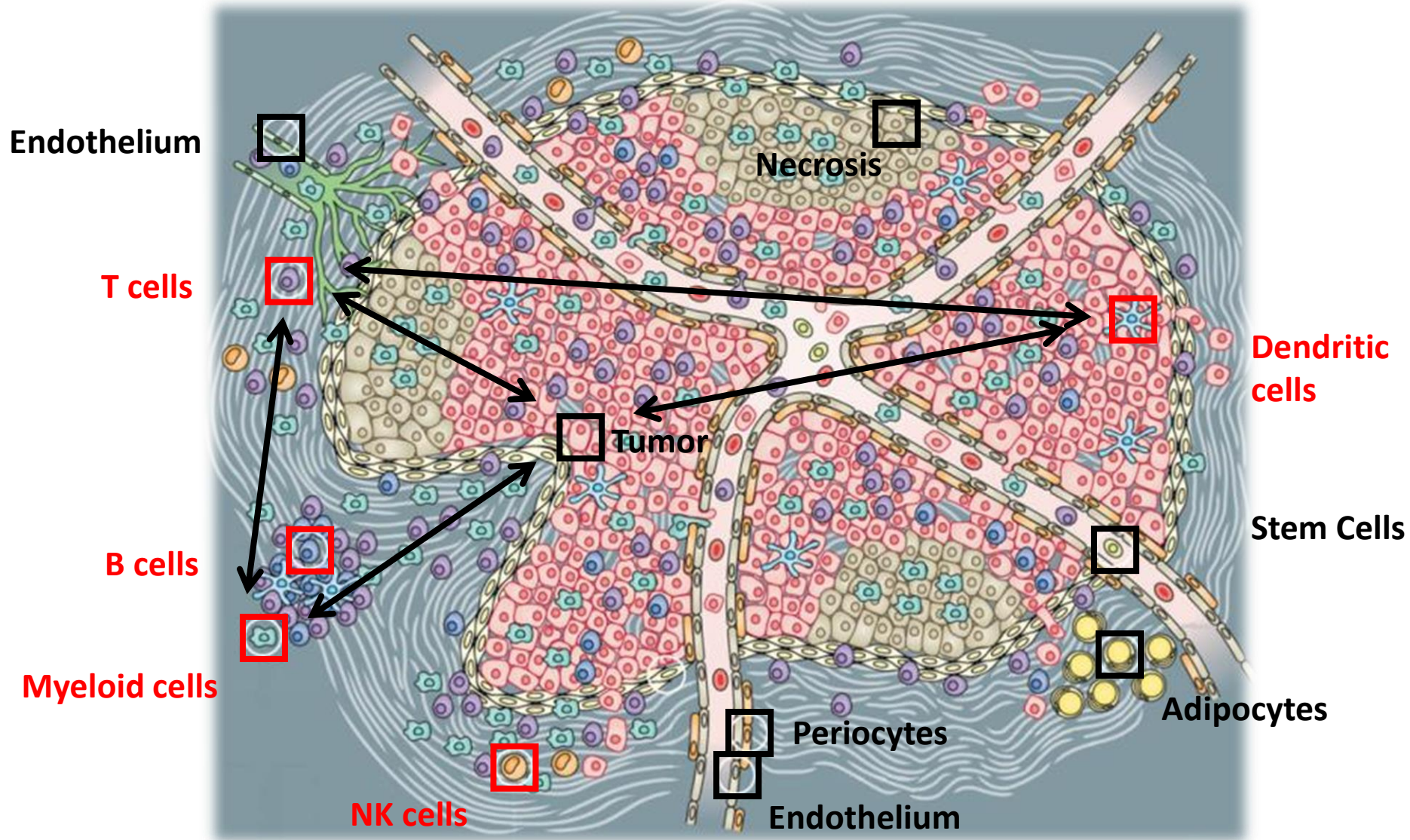
- Stage 2B worse than 3A. Stage 2C worse than stage 3A and 3B
- Complete staging frequently not performed
- Requires expert pathologists
- Provides estimates of survival that are difficult to plan care around (Stage IIB- 82%)
- Does not account for role of immune system in tumor progression

Adjuvant Therapy Works...But Who Should Receive it?



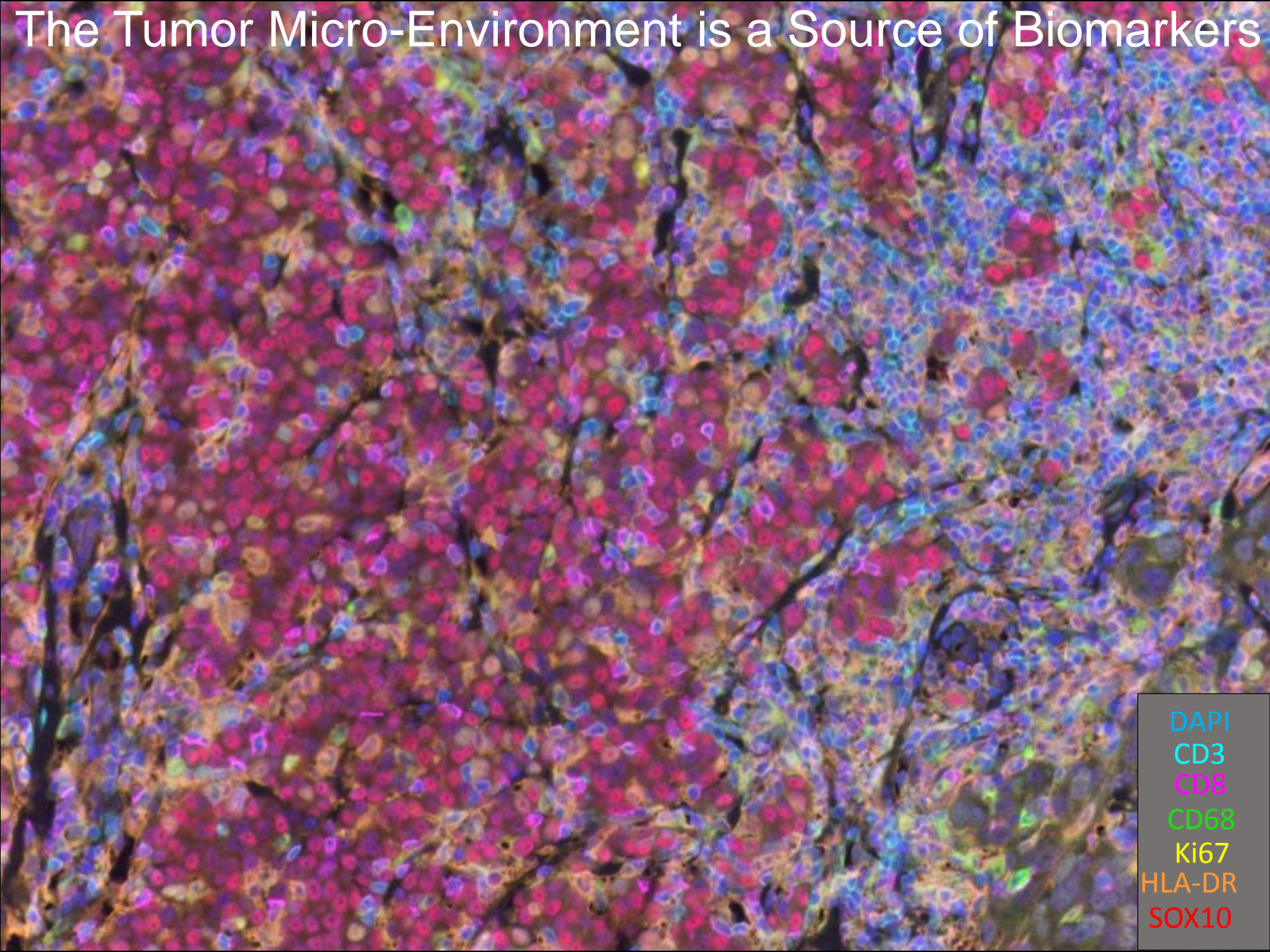
- Window of benefit in Stage 3 is narrow
- Most will do well regardless
- \$200,000 per patient and serious toxicity risks
- Large trials in Stage II patients without biomarkers underway. Over 70% will never recur
- PDL1 staining is not predictive of benefit

The Tumor Micro-Environment is a Source of Biomarkers



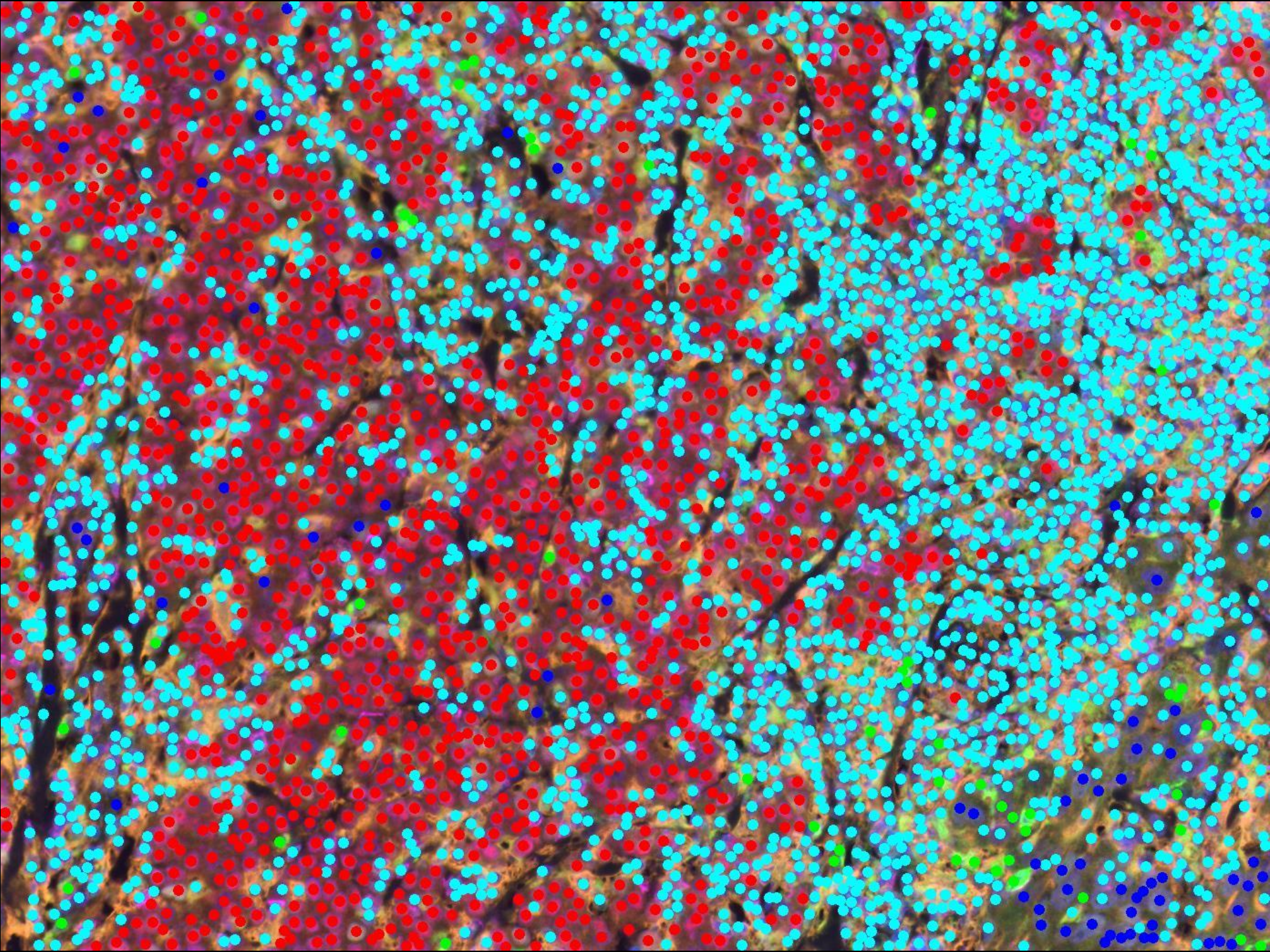
Adapted from Balkwill, et al, 2012.

The Tumor Micro-Environment is a Source of Biomarkers



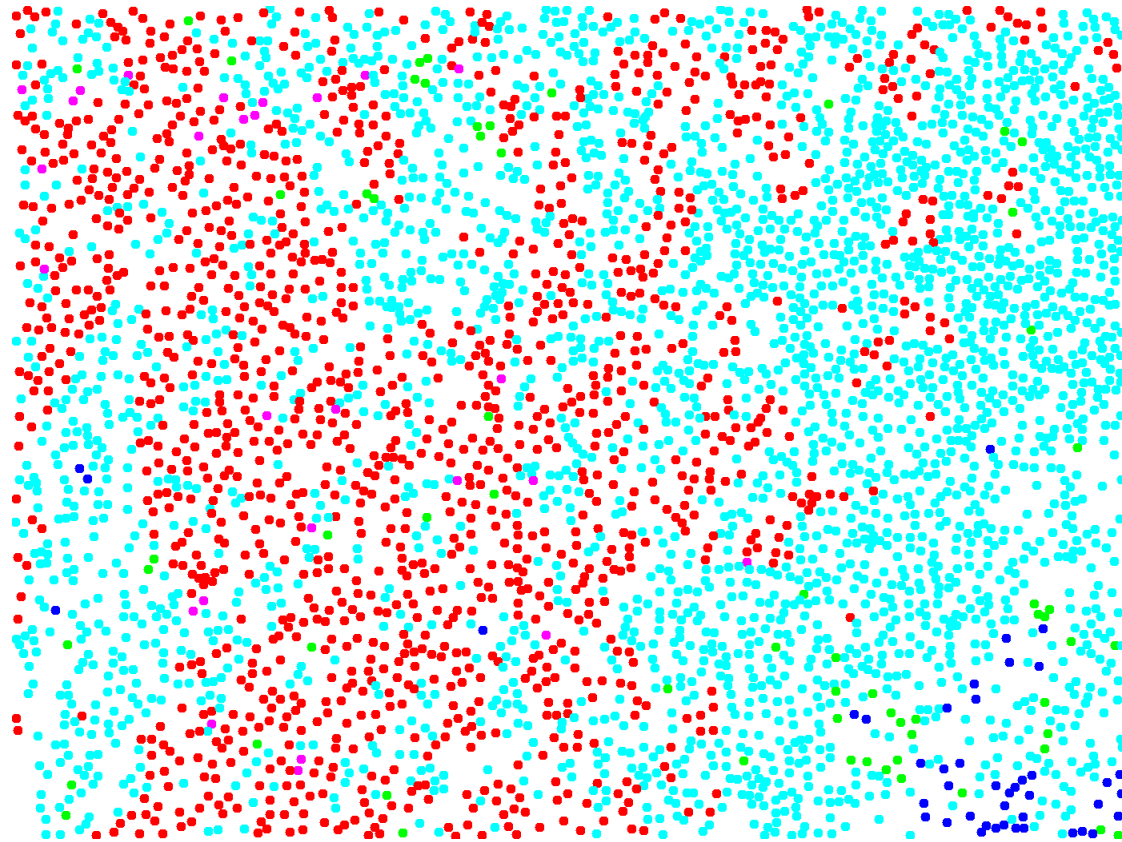
DAPI
CD3
CD8
CD68
Ki67
HLA-DR
SOX10

*Adapted from
Saenger et al CIR
2018; 6(4):491-
493*

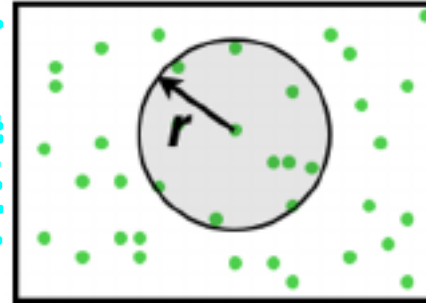


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Saenger et al CIR
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493*

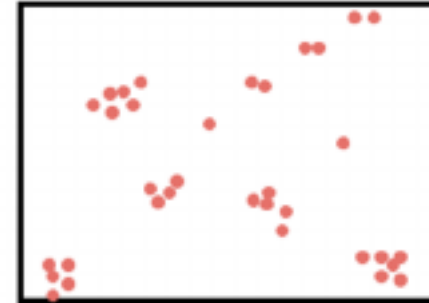
Abstraction of cell phenotypes as dots allows for mathematical analysis of spatial relationships



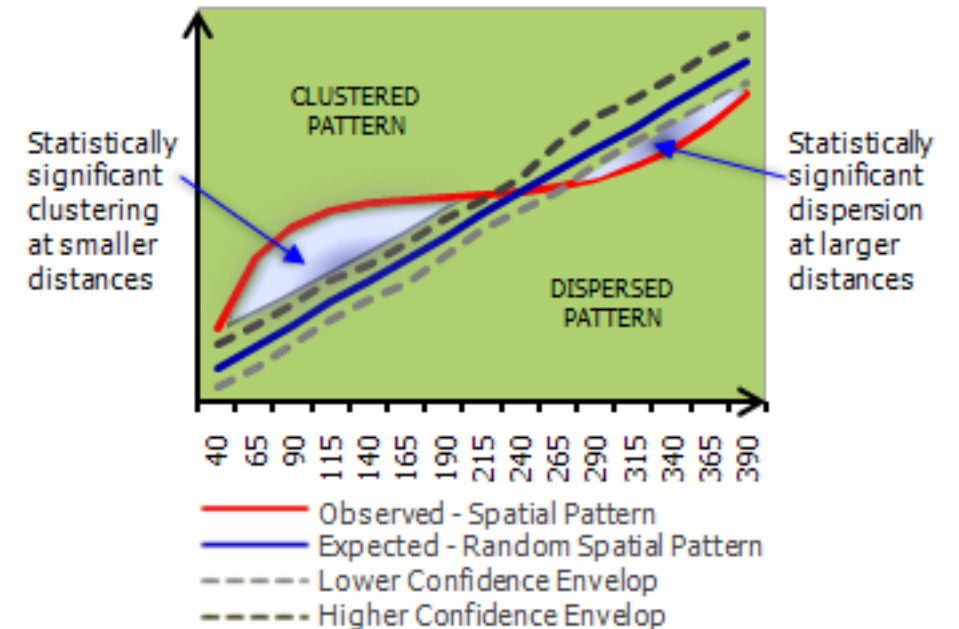
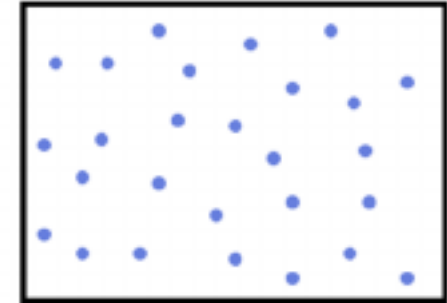
Uniform



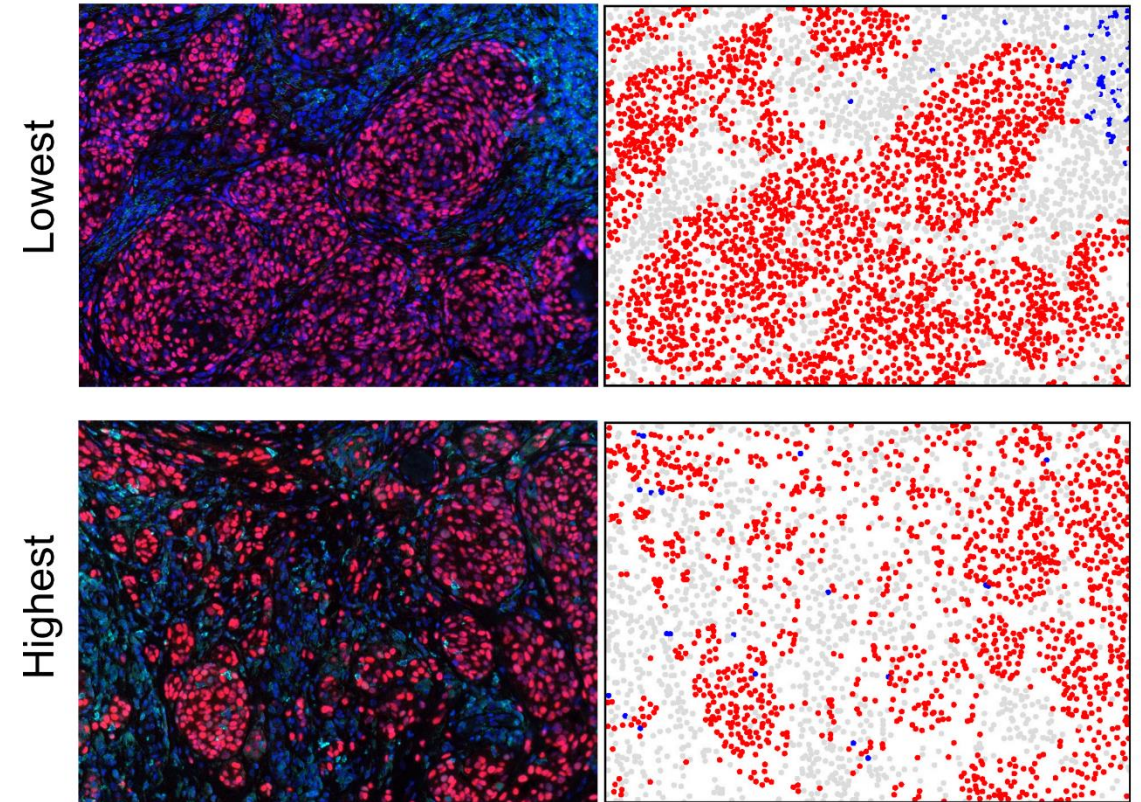
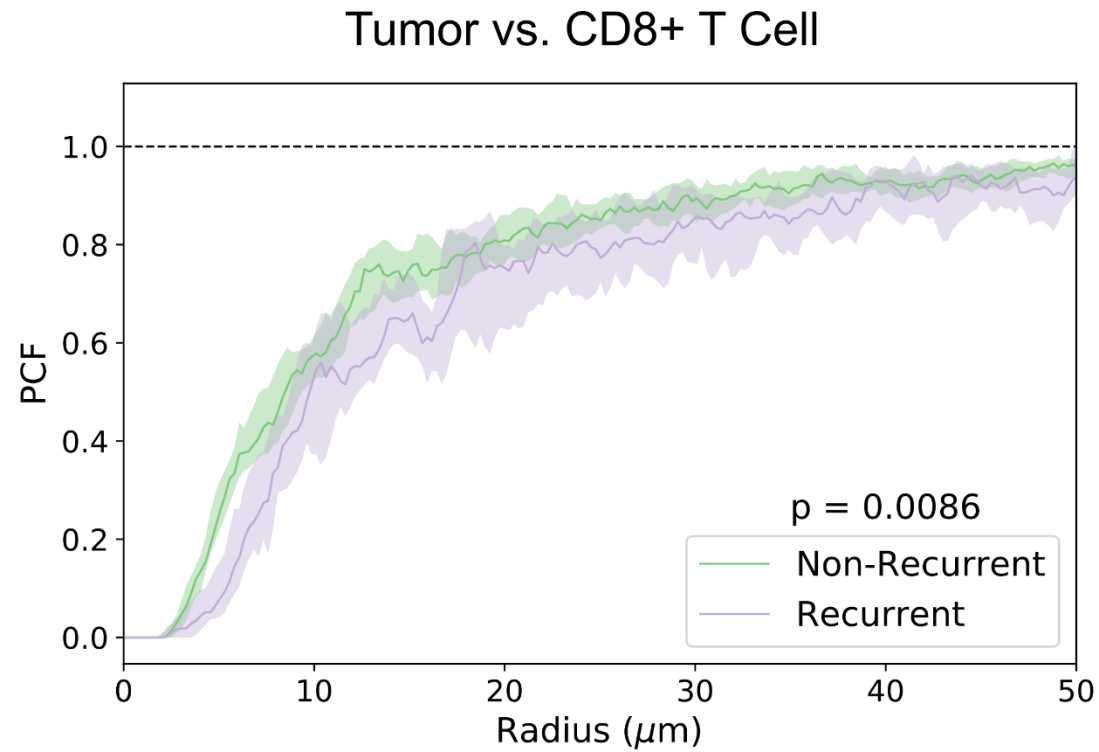
Clustered



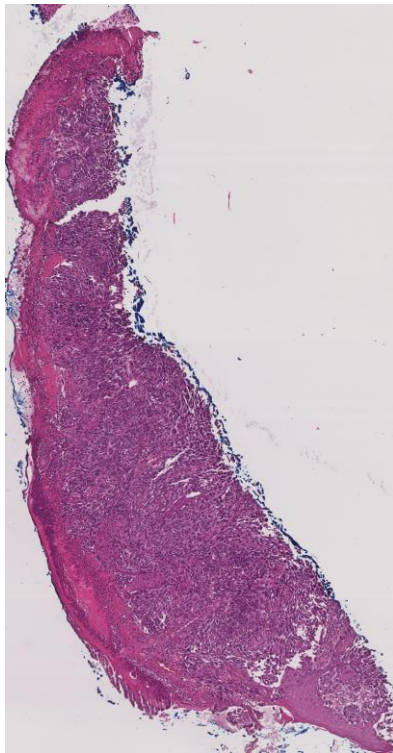
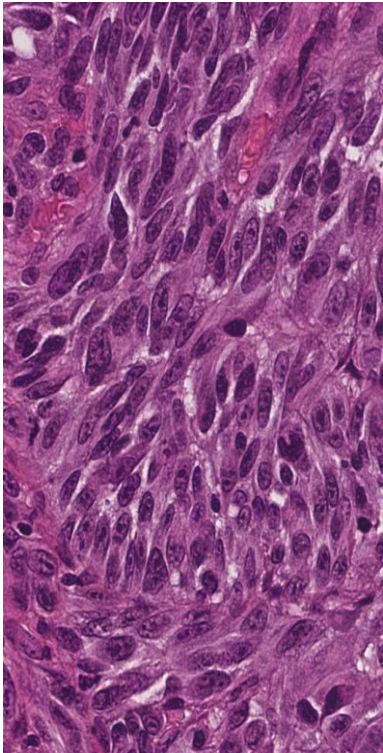
Dispersed



Paired Correlation Function Analysis Shows that Proximity of T cells to Tumor Cells Correlates with Recurrence Status



Overview of Our Approach



- Clinical and image data gathered from 3 medical centers (N=108)
- Cell-level information from QuPath (open-source pathology software)
- Image filtering and pre-processing of regional feature information
- Deep Learning Neural Network
- Majority voting from NN output

Training Population

(n = 108)		
Clinical characteristics		
Sex, n (%)		
Male	73	(67.6)
Female	34	(31.5)
Unknown	1	(0.9)
Age		
Known, n (%)	103	(95.4)
Median, n (range)	67	(22-96)
Unknown, n (%)	5	(4.6)
Location of tumor, n (%)		
Trunk	58	(53.7)
Extremity	48	(44.4)
Unknown	2	(1.9)
T-stage, n (%)		
T1a or T1b	18	(16.7)
T2a	11	(10.2)
T2b or T3a	41	(38.0)
T3b or T4a	22	(20.4)
T4b	12	(11.1)
Unknown	4	(3.7)
Stage, n (%)		
I	22	(20.4)
II	62	(57.4)
III	24	(22.2)

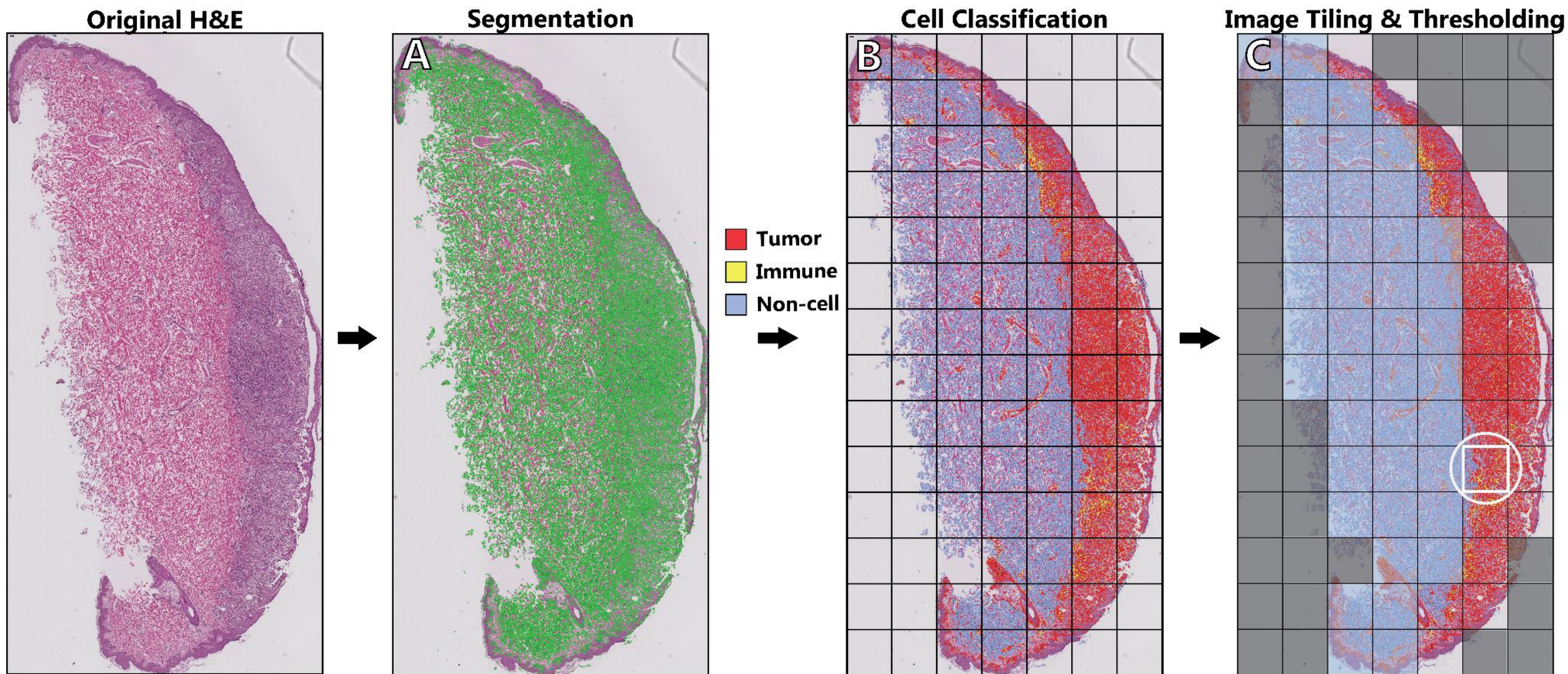
Pathologic characteristics

Depth (mm)	
Median, n (range)	2.30 (0.30-30)
Ulceration, n (%)	
Absent	57 (52.8)
Present	47 (43.5)
Unknown	4 (3.7)
Microsatellite lesions, n (%)	
Absent	101 (93.5)
Present	6 (5.6)
Unknown	1 (0.9)
TILs	
Absent	9 (8.3)
Non-brisk	67 (62.0)
Brisk	23 (21.3)
Unknown	9 (8.3)
SLNB status, n (%)	
Completed	66 (61.1)
Positive, n (% of completed)	20 (18.5)
Negative, n (% of completed)	46 (42.6)

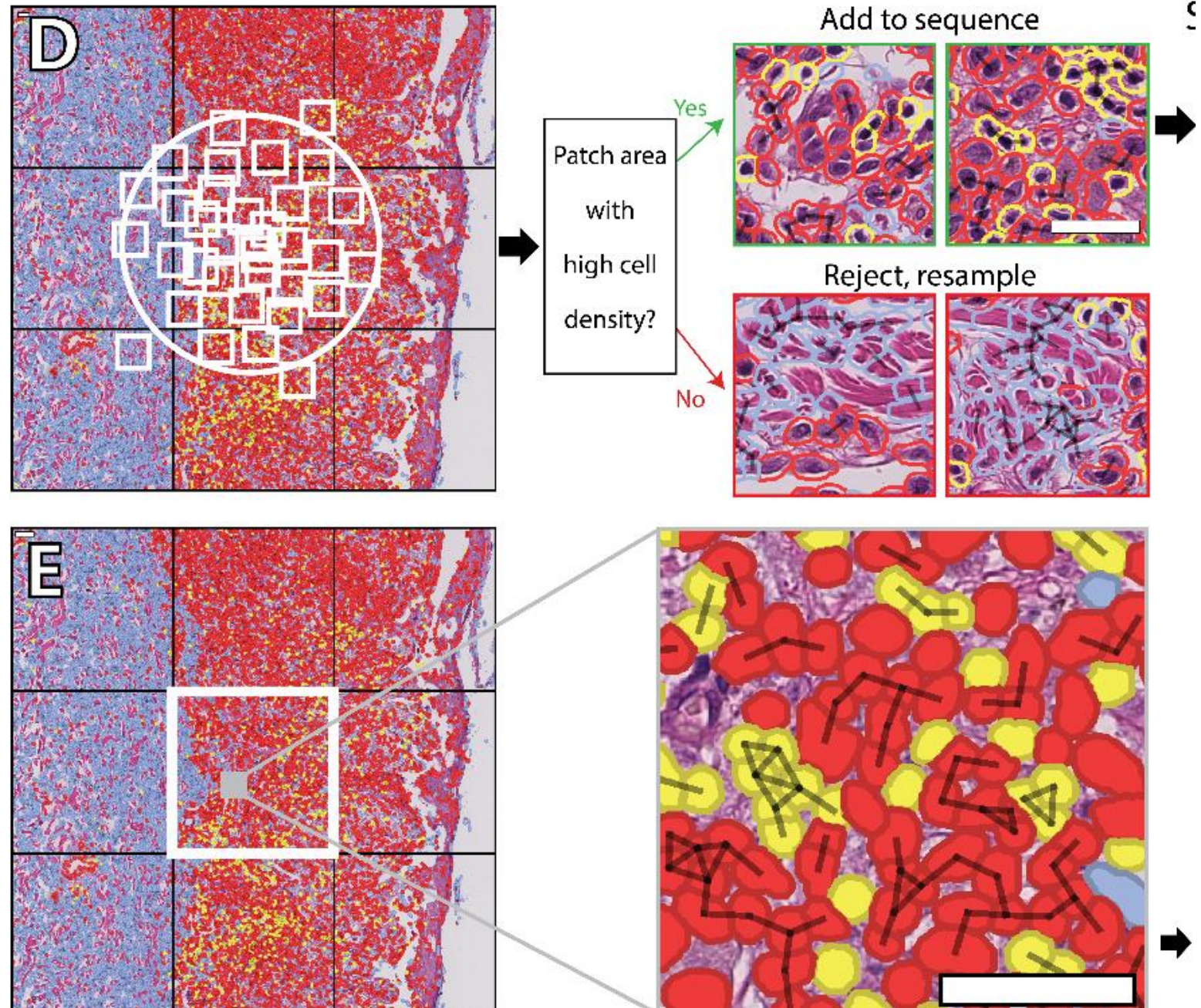
Outcome characteristics

Patient follow-up (months)	
Median, n (range)	58 (7-173)
DMR, n (%)	
Distant recurrence	34 (31.5)
No recurrence or local recurrence only	74 (68.5)
OS, n (%)	
Alive (at least 2 years)	69 (63.9)
Dead	39 (36.1)
DSS, n (%)	
Alive or NED at death	78 (72.2)
Median follow-up (months)	65
Dead with melanoma	30 (27.8)
Median follow-up (months)	34.5

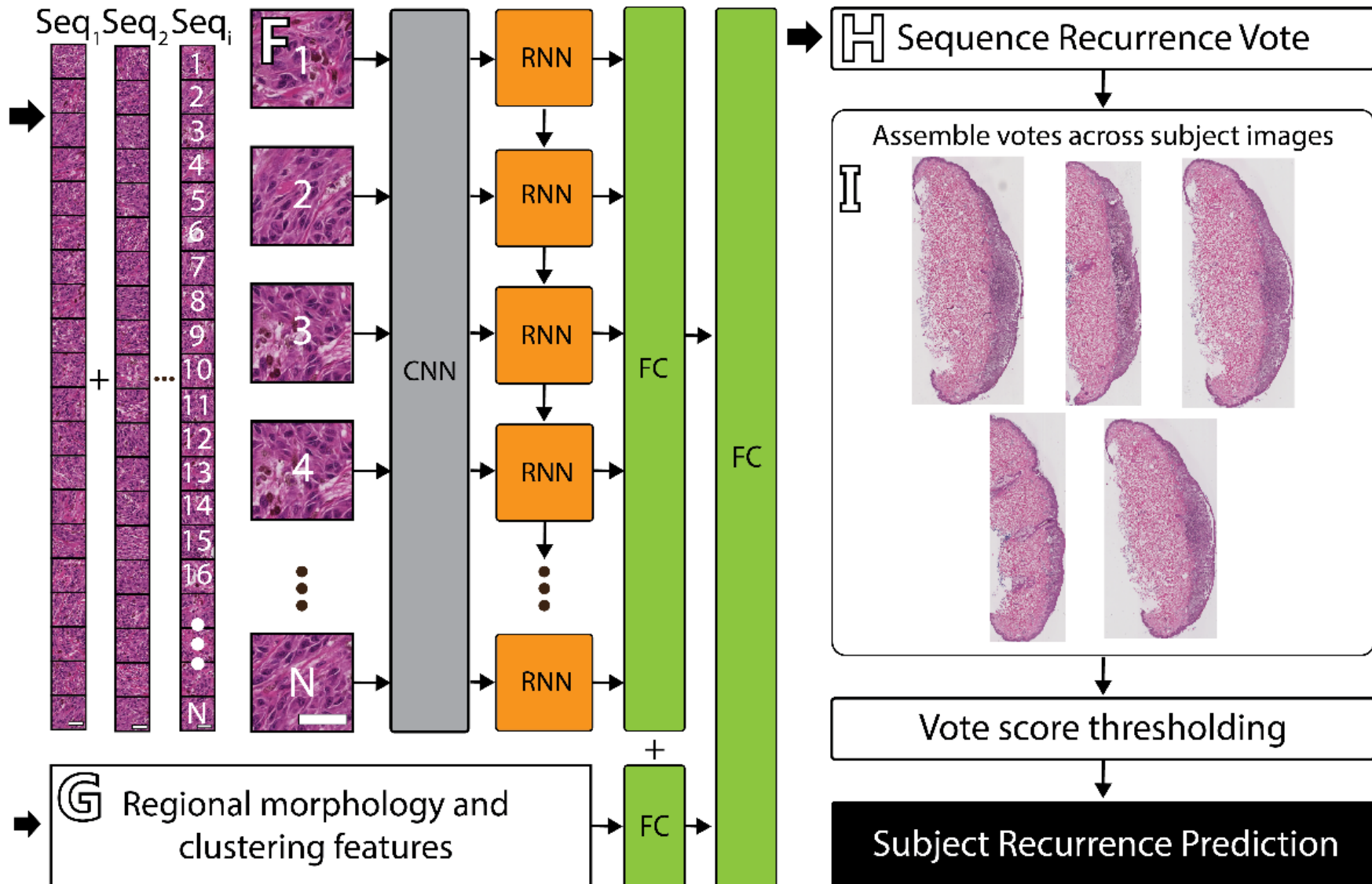
Tiling and Tile Selection



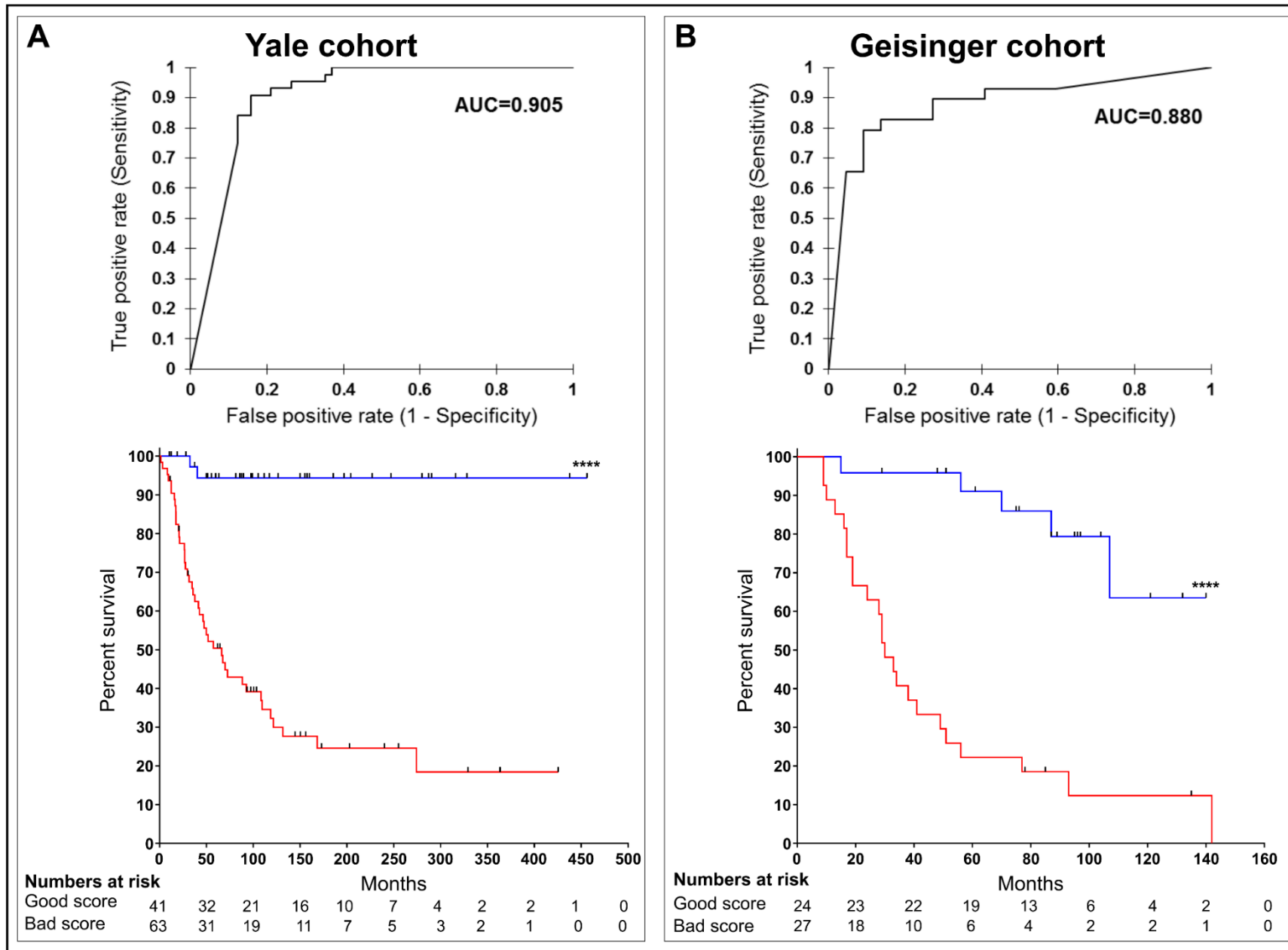
Patch Selection and Feature Generation



Sequence Generation and Network analysis



Validation on Two Independent Test Sets



Saenger et al. Clin.
Can. Res., 2019 Oct
21 Epub

Acknowledgements

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