

Using artificial intelligence to distinguish subjects with prostate cancer (PCa) from benign prostate hyperplasia (BPH) through immunophenotyping of MDSCs and lymphocyte cell populations

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Society for Immunotherapy of Cancer

Disclosure Information

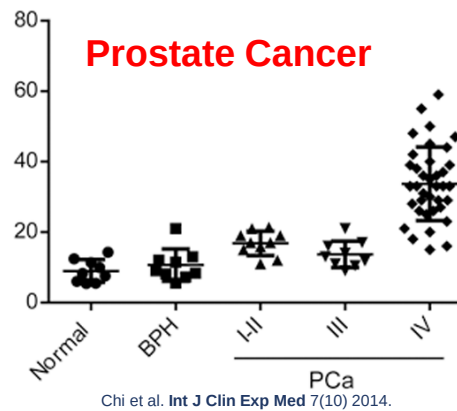
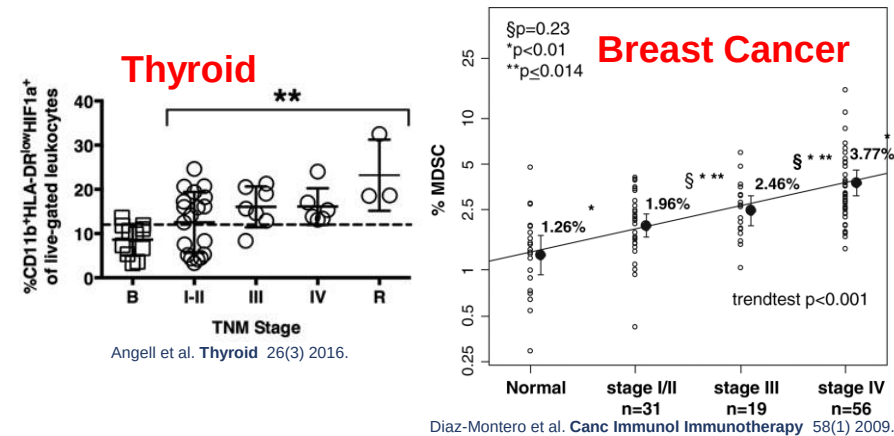
George Dominguez

Employee - Anixa Biosciences, Inc.

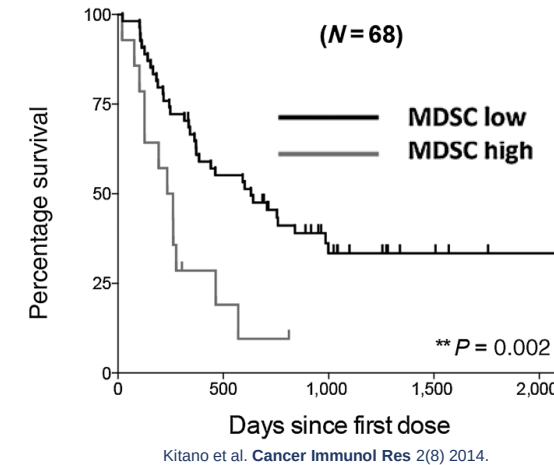
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What can MDSCs tell us?

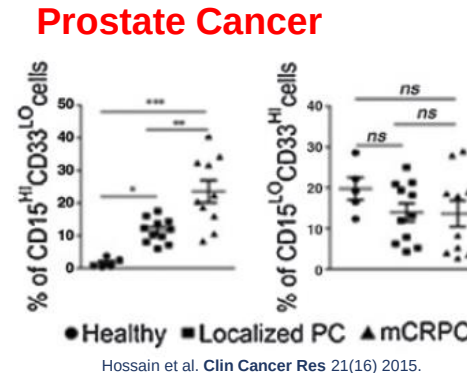
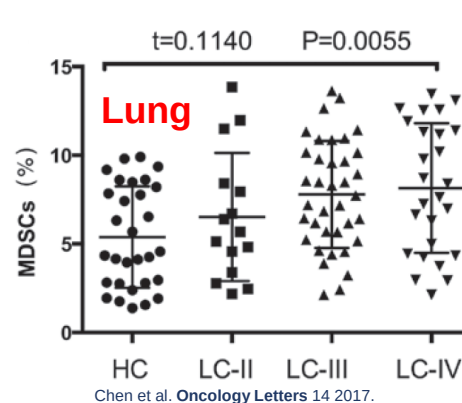
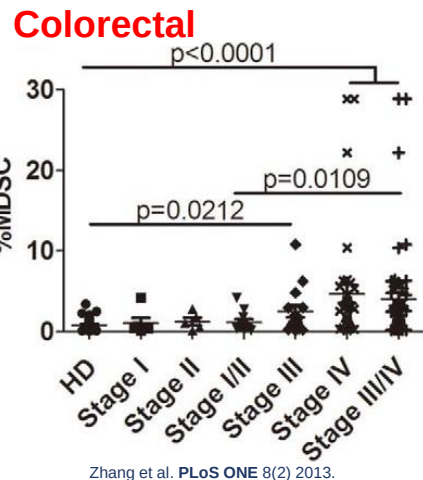
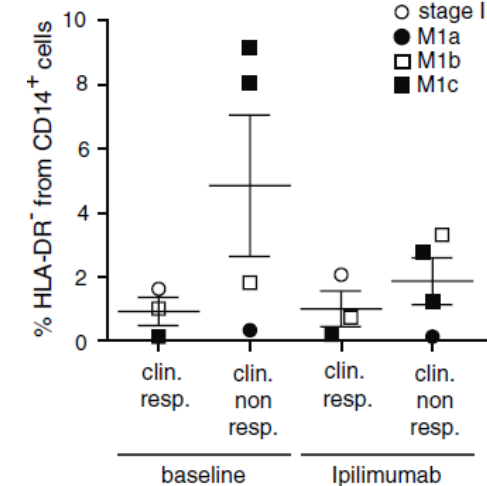
Indicative of Solid Tumors and Severity



Predictors of Immunotherapy Response?



CTLA-4 Responses in Late Stage Melanoma

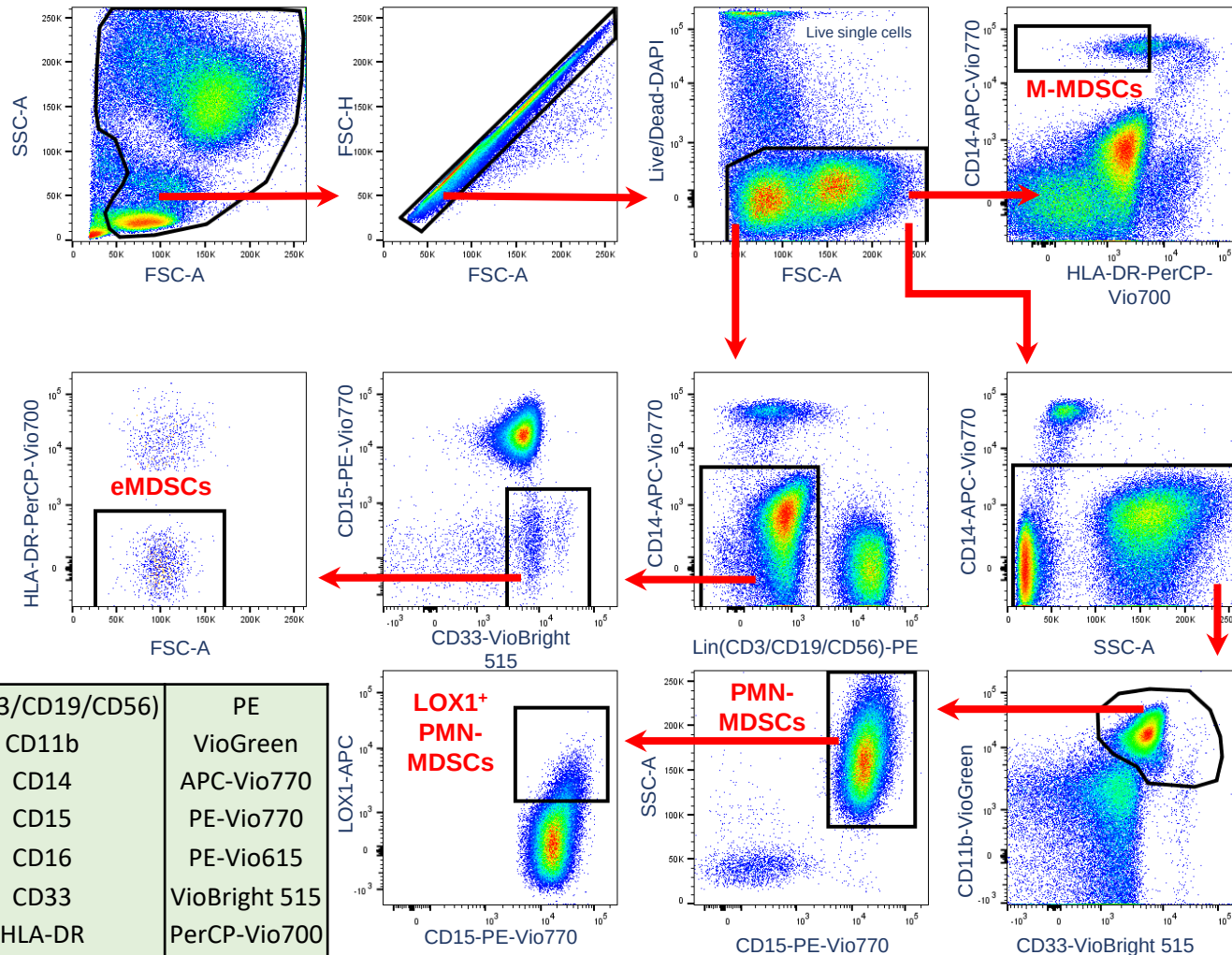


Question

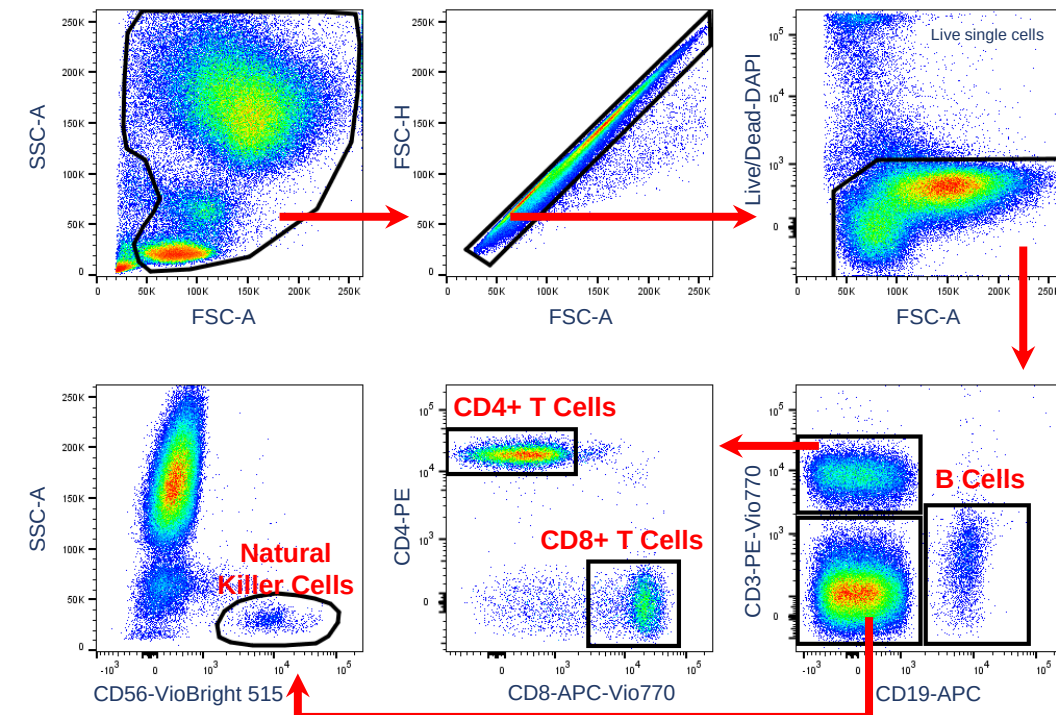
Can we use MDSCs as an indicator for higher risk prostate cancer (PCa) and distinguish from benign prostatic hyperplasia (BPH)/lower risk PCa?

What are we measuring?

Myeloid Panel (8 Markers)



Lymphoid Panel (5 Markers)



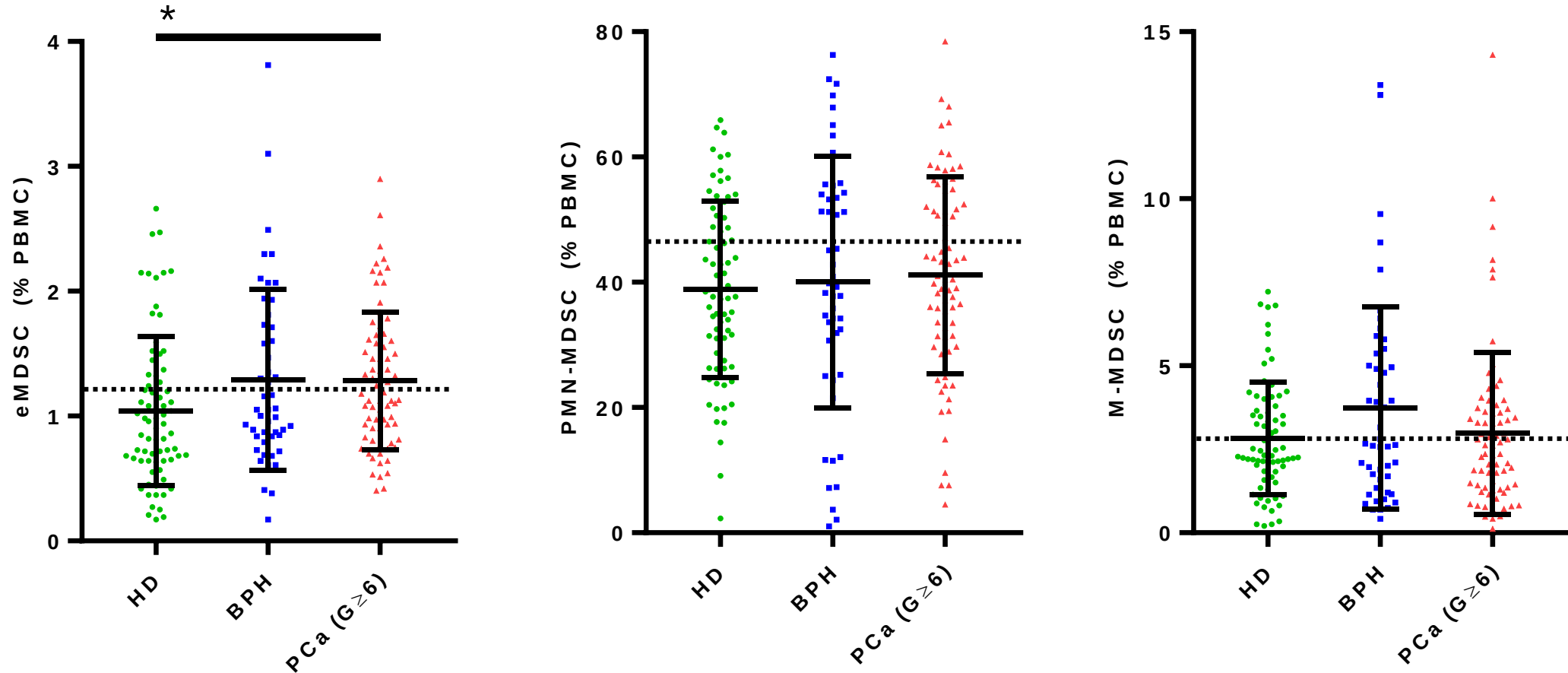
CD3	PE-Vio770
CD4	PE
CD8	APC-Vio770
CD19	APC
CD56	VioBright 515
Live/Dead	DAPI

Clinical Characteristics and Categorization

- Prospective blood collection – processed within 20 – 30 hours
- All subjects were already scheduled to undergo a transrectal ultrasound guided prostate (TRUSP) biopsy
- Subjects not included if they had:
 - previous history of cancer (excluding active surveillance)
 - any previous medical intervention for Pca
 - on active treatment for BPH

Characteristic	PCa	BPH	HD
Total	73	48	73
Median Age	65	62	53
Age Range	44 - 86	40 - 81	22 - 79
Gleason Score			
6	26		
7 (3+4)	14		
7 (4+3)	15		
>8	18		
Tumor Stage			
T1c	43		
T2a	2		
Unknown	28		

Traditional Gating: Manual Counting - MDSCs



Simple cell counts can provide information about trends, but can only categorize some subjects

Healthy Donor (HD) n = 73

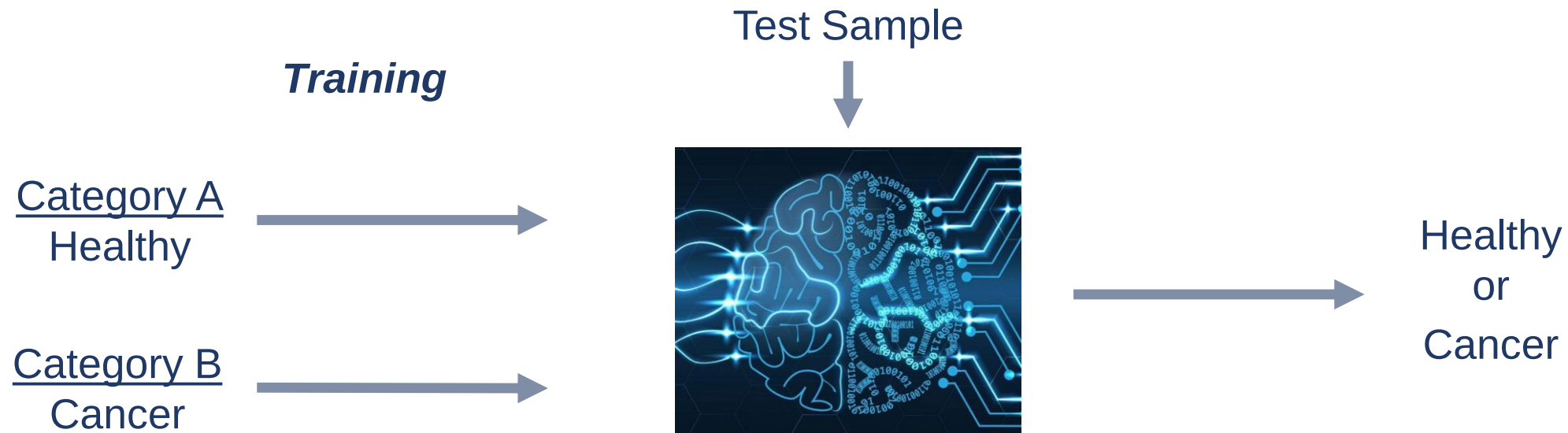
Benign Prostatic Hyperplasia (BPH) n = 48

Prostate Cancer (PCa) n = 73

*The dotted line represents the 75th percentile for HD values (75% specificity)

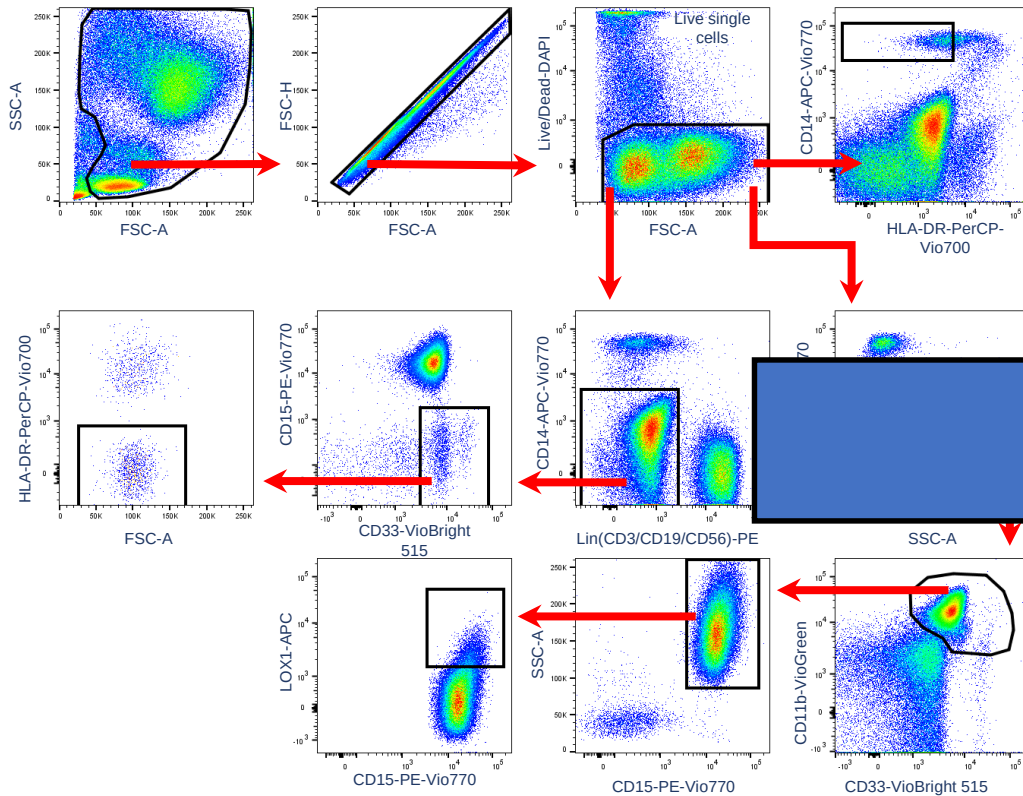
Our Question

Can we use machine learning (neural networks) to analyze the flow cytometry data to categorize patients?

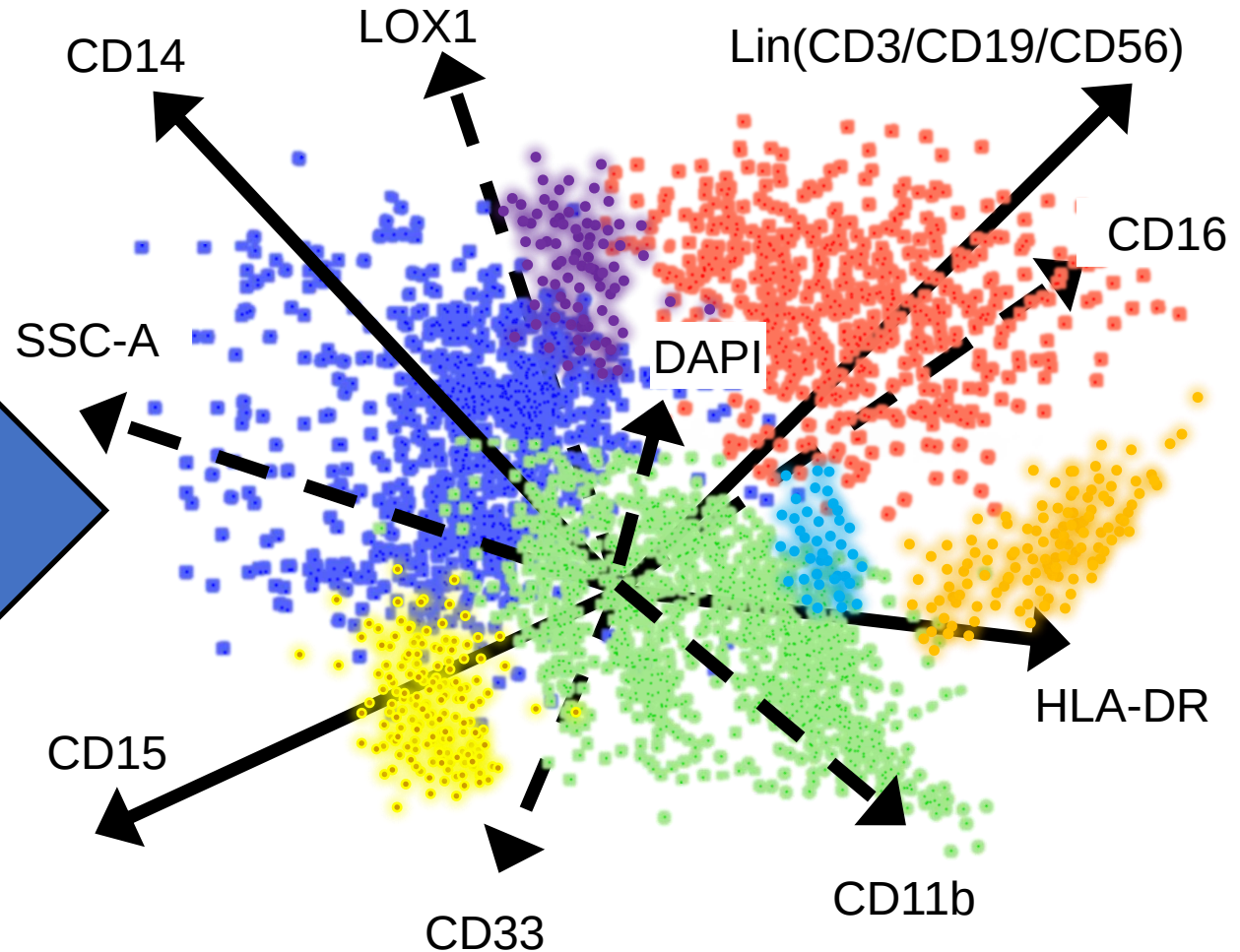


The Inputs – Event Counts

FCS File → CSV File (Event counts for each channel)



Multidimensional Space

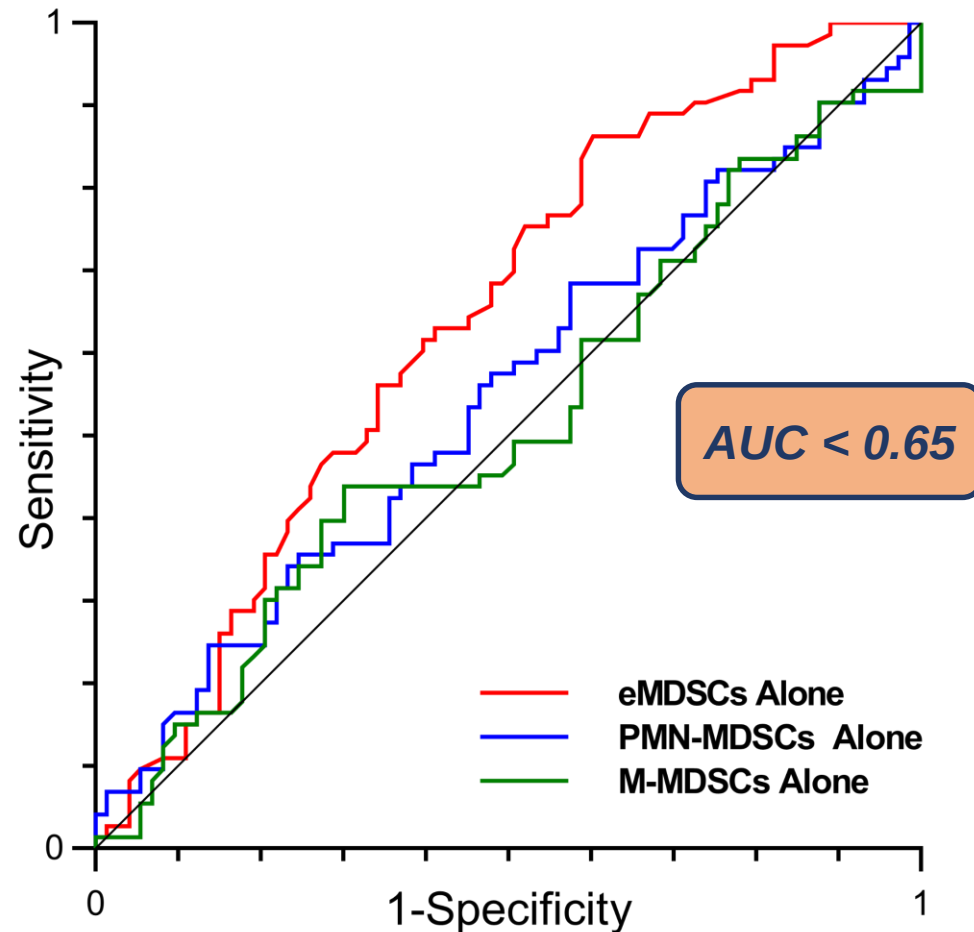


The Neural Network does not see gates, markers, or fluorophores – it just sees numbers

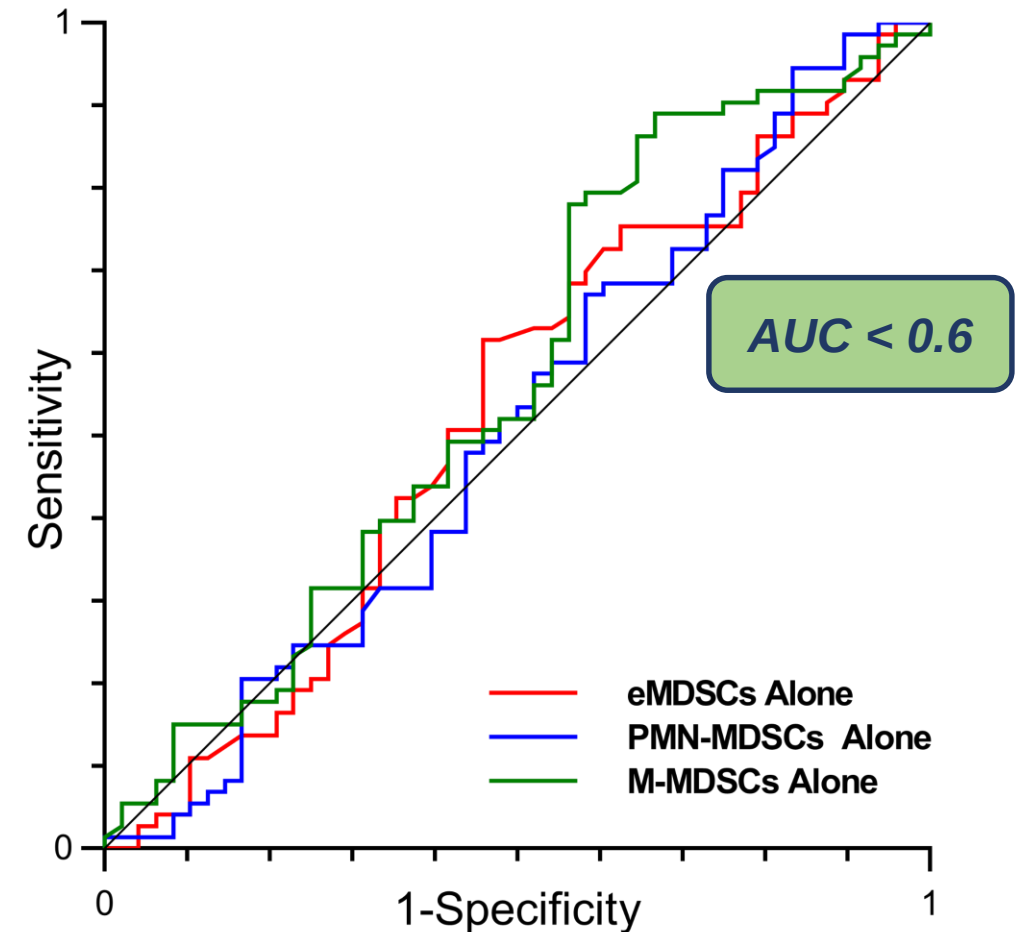
Manual Gating – not enough...

*PCa (Adenocarcinoma) = Gleason ≥ 6

Healthy Donor vs Prostate Cancer



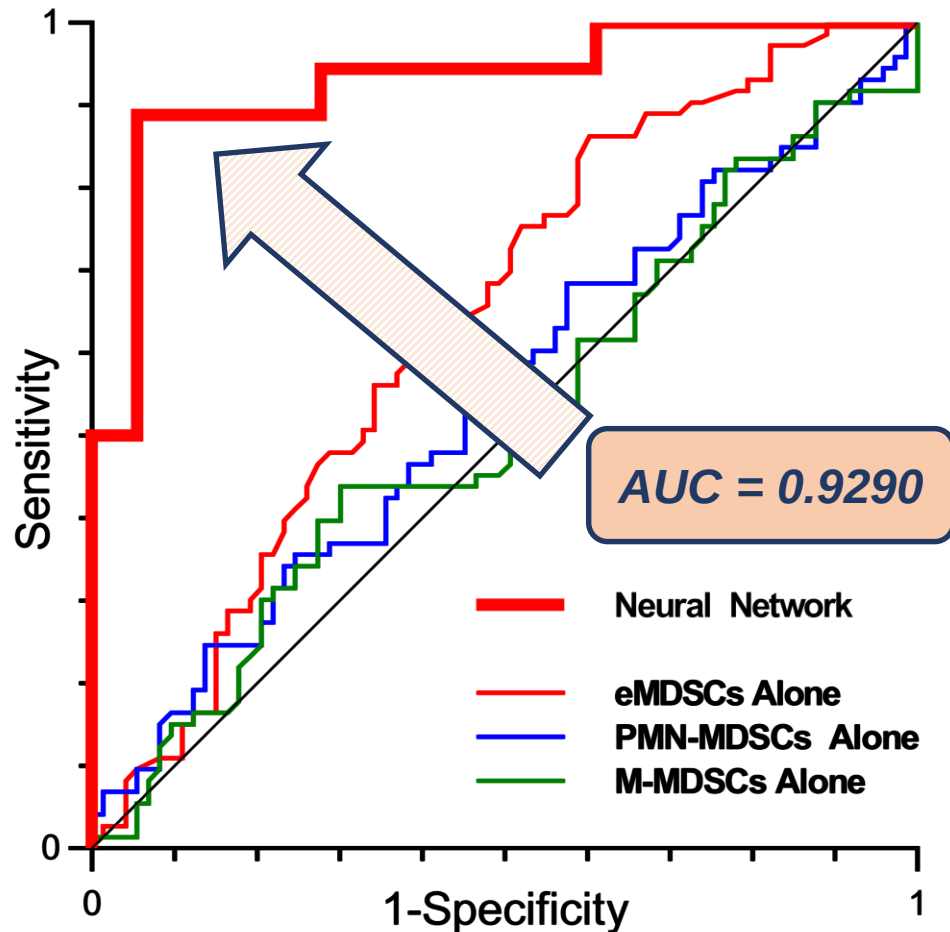
BPH vs Prostate Cancer



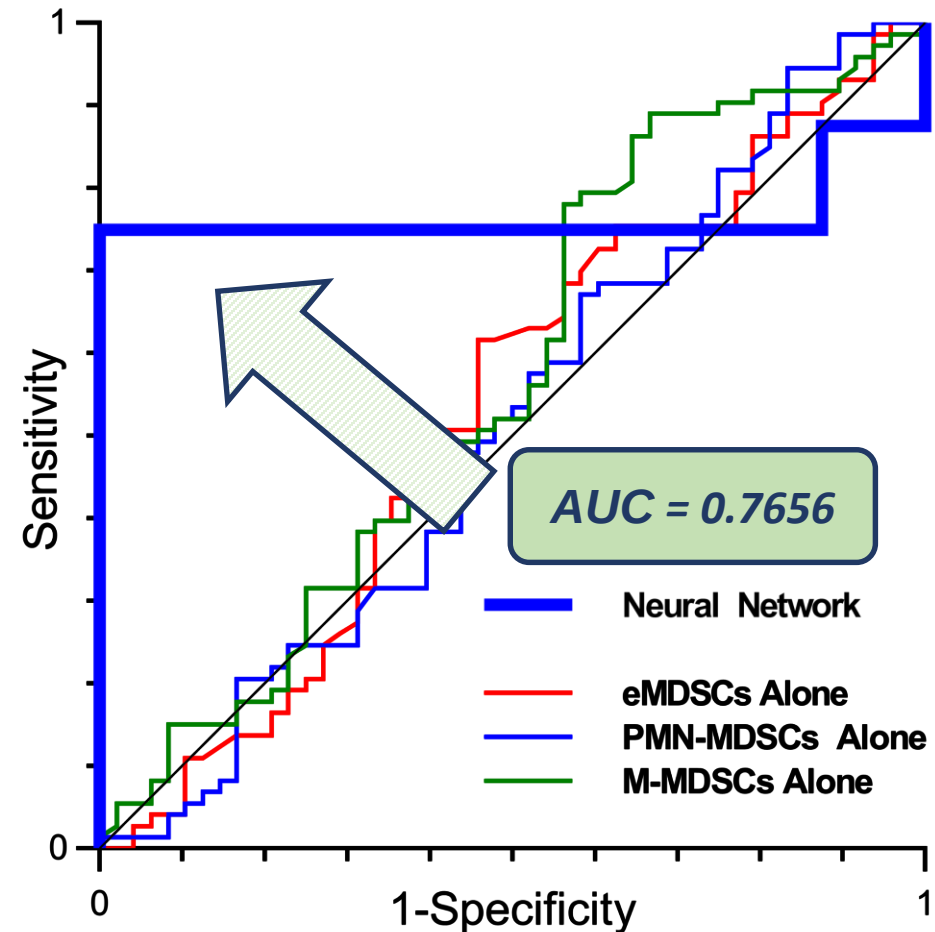
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Healthy Donor vs Prostate Cancer



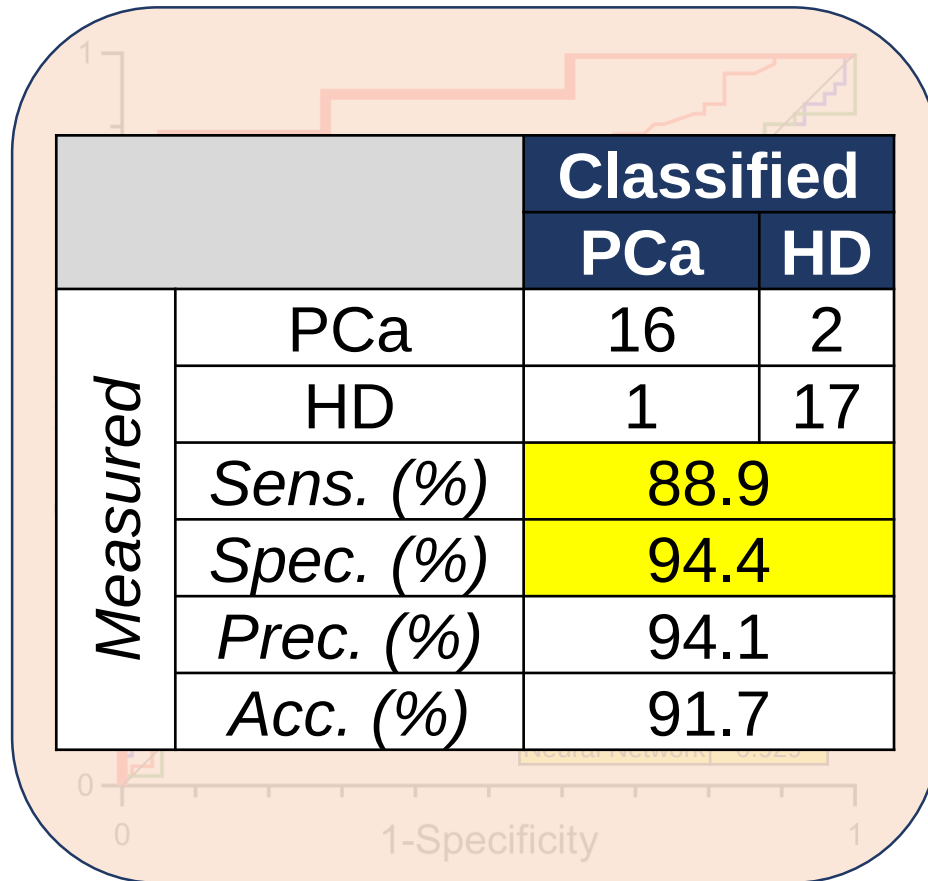
BPH vs Prostate Cancer



Using a Neural Network is Superior

*PCa (Adenocarcinoma) = Gleason ≥ 6

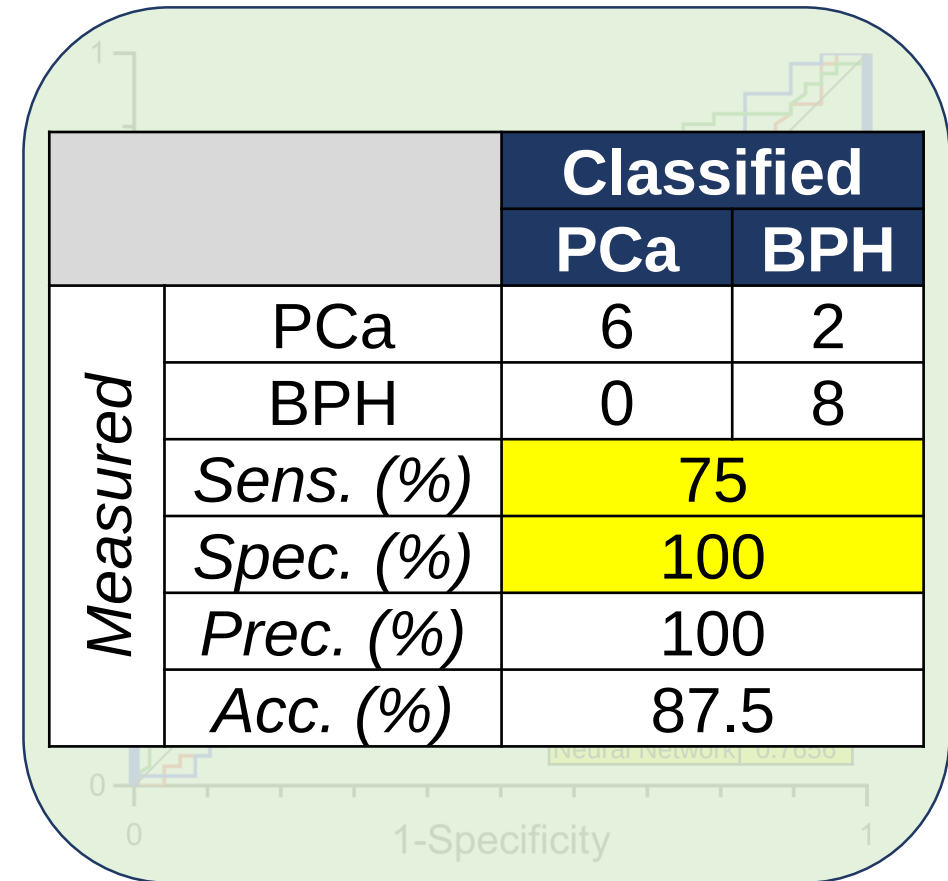
Healthy Donor vs Prostate Cancer



A Receiver Operating Characteristic (ROC) curve plot for the classification of Prostate Cancer (PCa) versus Healthy Donor (HD). The x-axis is labeled '1-Specificity' and ranges from 0 to 1. The y-axis is labeled 'Sensitivity' and ranges from 0 to 1. A red step-like curve is plotted, starting at (0,0) and ending at (1,1), indicating high performance. The curve is above the diagonal line, showing good discrimination between the two classes.

		Classified	
		PCa	HD
Measured	PCa	16	2
	HD	1	17
	Sens. (%)	88.9	
	Spec. (%)	94.4	
	Prec. (%)	94.1	
	Acc. (%)	91.7	

BPH vs Prostate Cancer



A Receiver Operating Characteristic (ROC) curve plot for the classification of Prostate Cancer (PCa) versus Benign Prostatic Hyperplasia (BPH). The x-axis is labeled '1-Specificity' and ranges from 0 to 1. The y-axis is labeled 'Sensitivity' and ranges from 0 to 1. A red step-like curve is plotted, starting at (0,0) and ending at (1,1), indicating high performance. The curve is above the diagonal line, showing good discrimination between the two classes.

		Classified	
		PCa	BPH
Measured	PCa	6	2
	BPH	0	8
	Sens. (%)	75	
	Spec. (%)	100	
	Prec. (%)	100	
	Acc. (%)	87.5	

What is a clinical application of this technology?

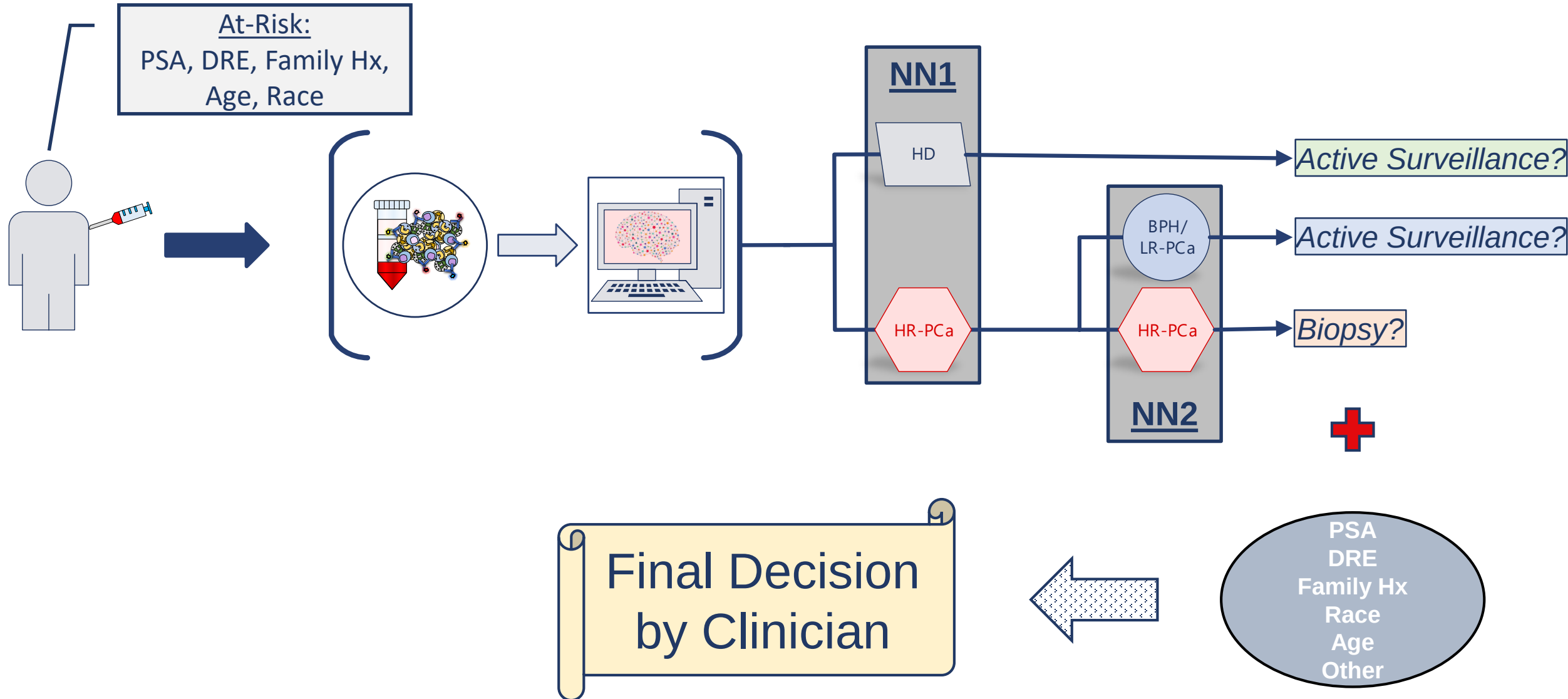
Clinical Application: Confirmatory Testing

- PSA is not reliable (large numbers of false positives)
- Majority of biopsies are negative
- 20% to 50% of men diagnosed through screening may be over diagnosed
- Gold Standard for Confirming → Prostate Biopsy (invasive/stressful)

Risks of Screening and Overdiagnosis/Overtreatment

- 1% of prostate biopsies result in hospitalization
- 1 in 5 men who undergo prostatectomy may develop long-term urinary incontinence
- 2 in 3 men may experience long-term erectile dysfunction
- 1 in 6 men may experience long-term bothersome bowel symptoms

Clinical Application: Confirmatory Testing for PCa Bx

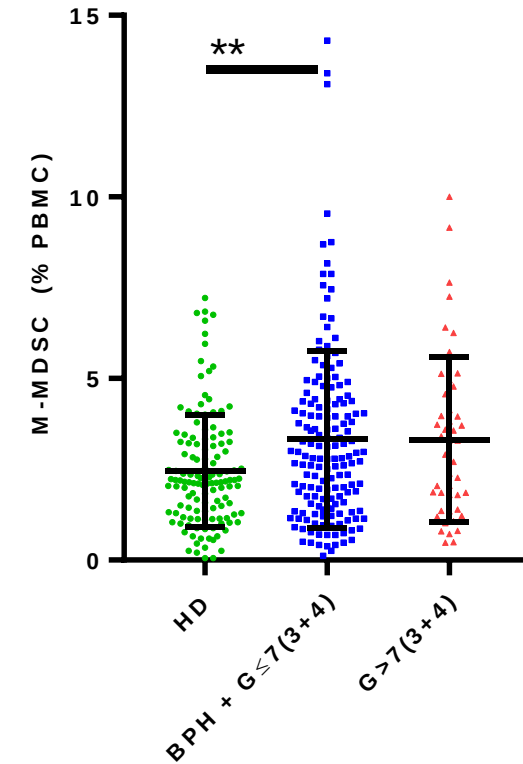
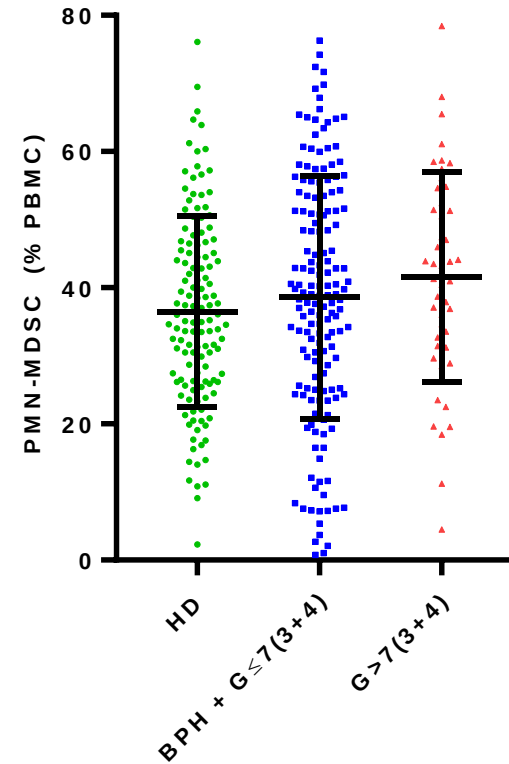
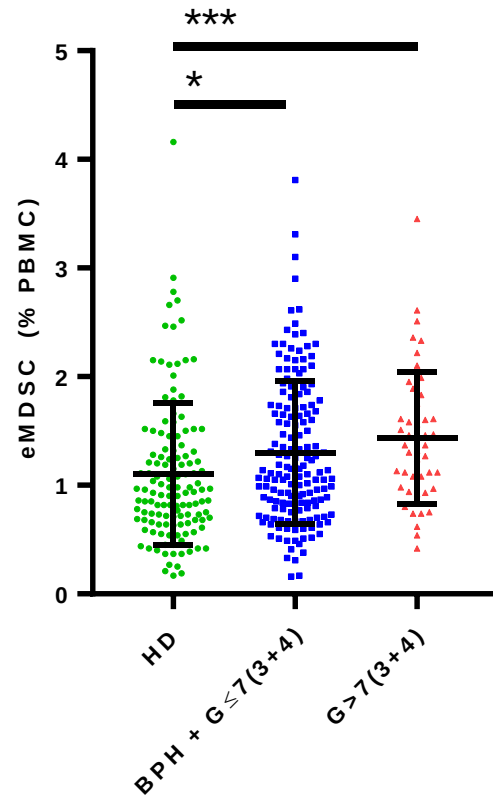


Clinical Characteristics and Manual Counting

➤ Additional samples were collected

- + 41 PCa
- + 41 BPH
- + 43 Male HD

Characteristic	PCa	BPH	HD
Total	114	89	116
Median Age	67	62	52
Age Range	42 – 86	40 – 81	18 – 79
Gleason Score			
6	44		
7 (3+4)	26		
7 (4+3)	22		
>8	22		
Tumor Stage			
T1c	75		
T2a	5		
T2c	2		
Unknown	32		



Still...simple cell counts can provide information about trends, but not really categorize subjects

Clinical Application: Confirmatory Testing

		Classified	
		Biopsy Recommended	Biopsy Not Recommended
Measured	Needs Biopsy	9	1
	Does Not Need Biopsy	24	26
	Sens. (%)	90	
	Spec. (%)	52	
	Prec. (%)	27.27	
	Acc. (%)	58.33	

Gleason $\geq 7(4+3)$

Gleason $\leq 7(3+4)$
+ BPH

- Classified 26 BPH/LR-PCa samples as “Biopsy Not Recommended” → potentially reduce the number of unnecessary biopsies
- Mis-classified 1 out of the 10 HR-PCa samples → other factors may still suggest biopsy
 - subject had an abnormal DRE and a PSA > 20 ng/ml

Conclusions

- We demonstrated that machine learning can be used to analyze flow cytometry data of MDSC and lymphocytes
- We have applied this technique to distinguish between HD/PCa and BPH/PCA in a small number of samples
- We also demonstrated that this has the potential to reduce the number of unnecessary prostate biopsies (confirmatory testing)
 - PSA results have high false positive rate
 - Over 1 million prostate biopsies performed annually - overwhelmingly negative

Future Work

- Incorporate DRE results? PSA? Age? Race?
- Identify the critical relationships between cell populations that are used to make the classifications → unexpected relationships?
- Can this technique be applied to other flow cytometer data sets with different cancers? (retrospective analysis)
- Can this be used for predicting tumor recurrence, treatment and/or immunotherapy responses?
 - Collaborative projects

Thank You!

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Questions?

Visit our poster (O2) tonight if you have more questions or interested in more details.