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

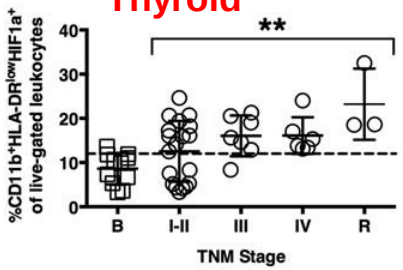
Employee - Anixa Biosciences, Inc.

Stock Options - Anixa Biosciences, Inc.

What can MDSCs tell us?

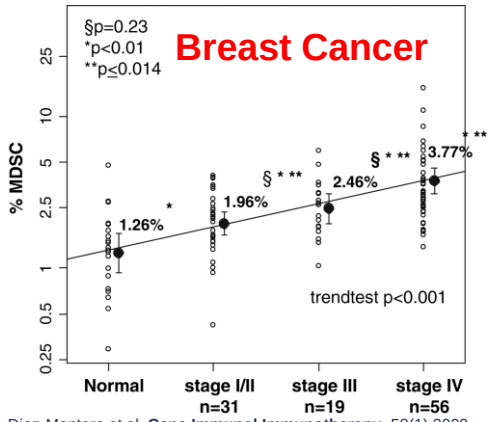
Indicative of Solid Tumors and Severity

Thyroid



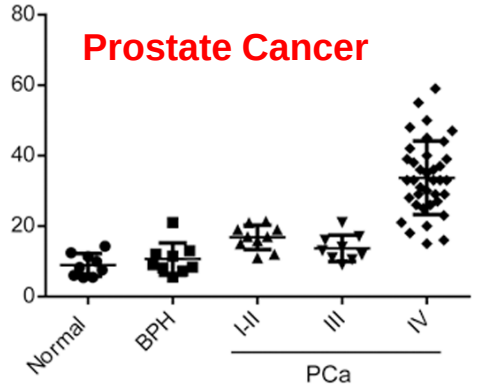
Angell et al. **Thyroid** 26(3) 2016.

Breast Cancer



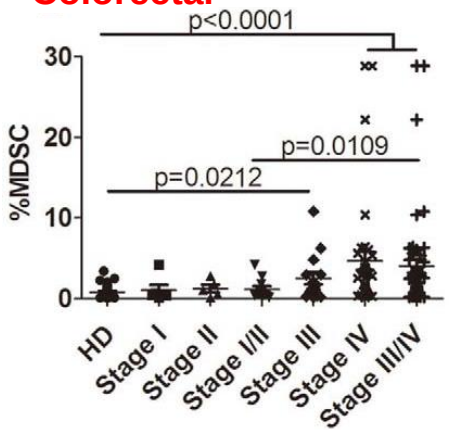
Diaz-Montero et al. **Canc Immunol Immunotherapy** 58(1) 2009.

Prostate Cancer



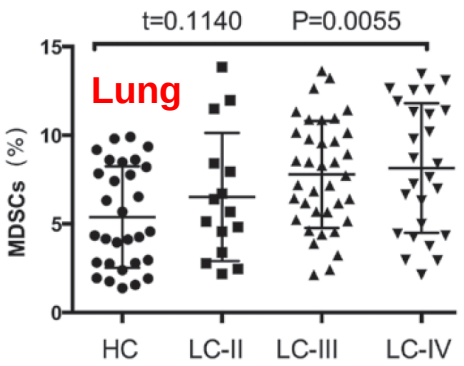
Chi et al. **Int J Clin Exp Med** 7(10) 2014.

Colorectal



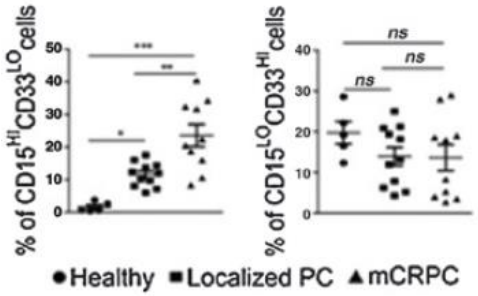
Zhang et al. **PLoS ONE** 8(2) 2013.

Lung



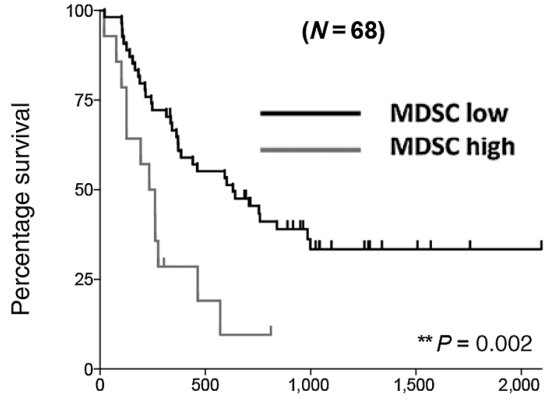
Chen et al. **Oncology Letters** 14 2017.

Prostate Cancer



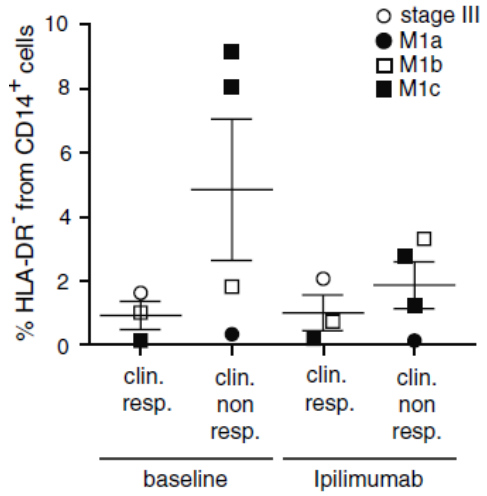
Hossain et al. **Clin Cancer Res** 21(16) 2015.

Predictors of Immunotherapy Response?



Kitano et al. **Cancer Immunol Res** 2(8) 2014.

CTLA-4 Responses in Late Stage Melanoma



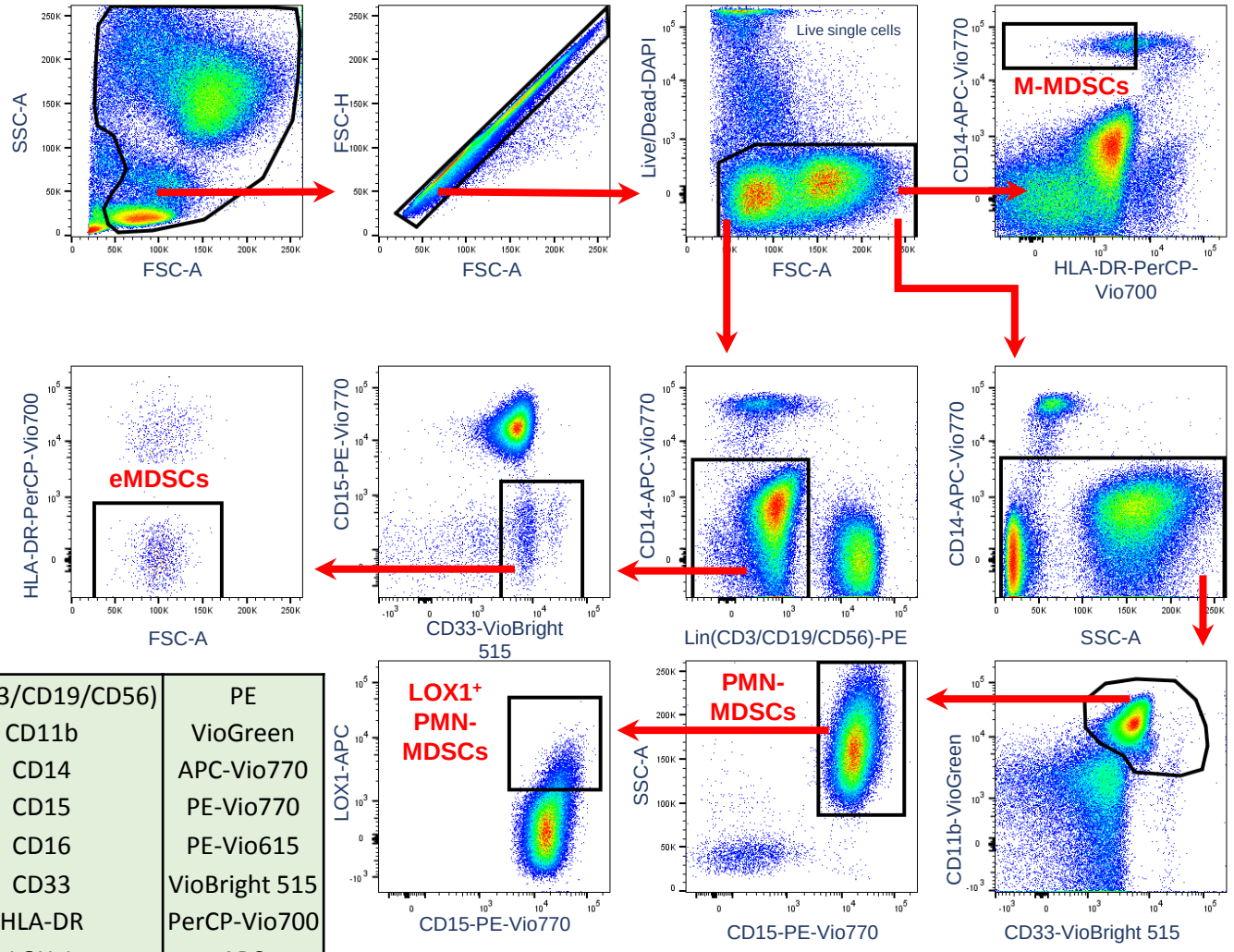
Meyer et al. **Cancer Immunol Immunother** 63:247-257 2014.

Question

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

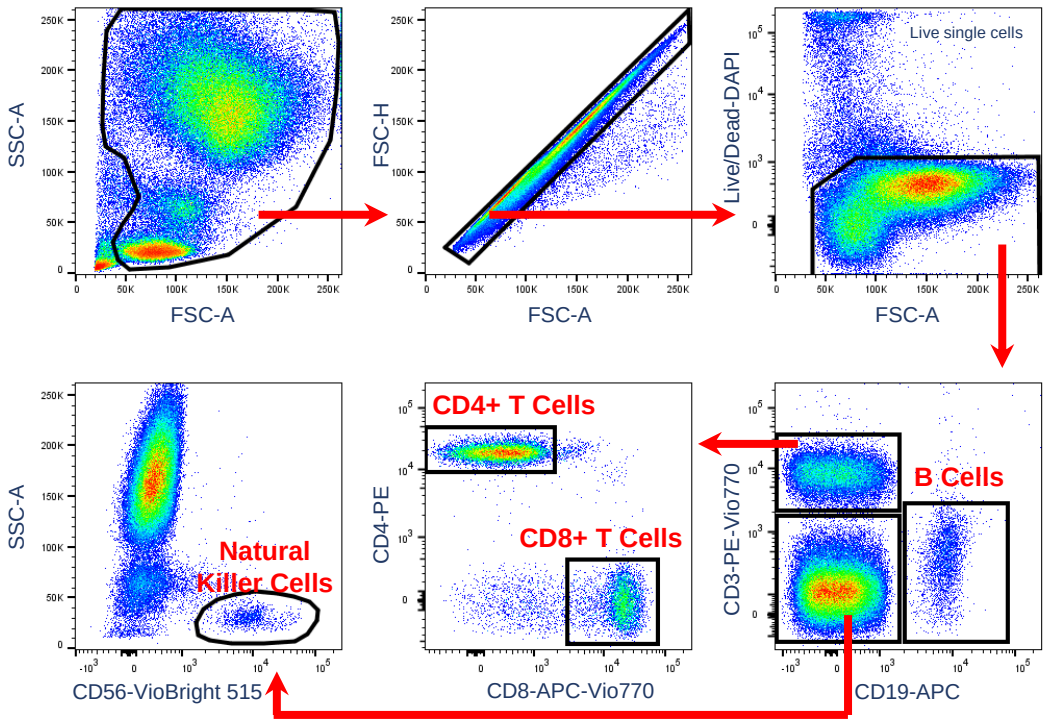
What are we measuring?

Myeloid Panel (8 Markers)



Lin(CD3/CD19/CD56)	PE
CD11b	VioGreen
CD14	APC-Vio770
CD15	PE-Vio770
CD16	PE-Vio615
CD33	VioBright 515
HLA-DR	PerCP-Vio700
LOX-1	APC
Live/Dead	DAPI

Lymphoid Panel (5 Markers)



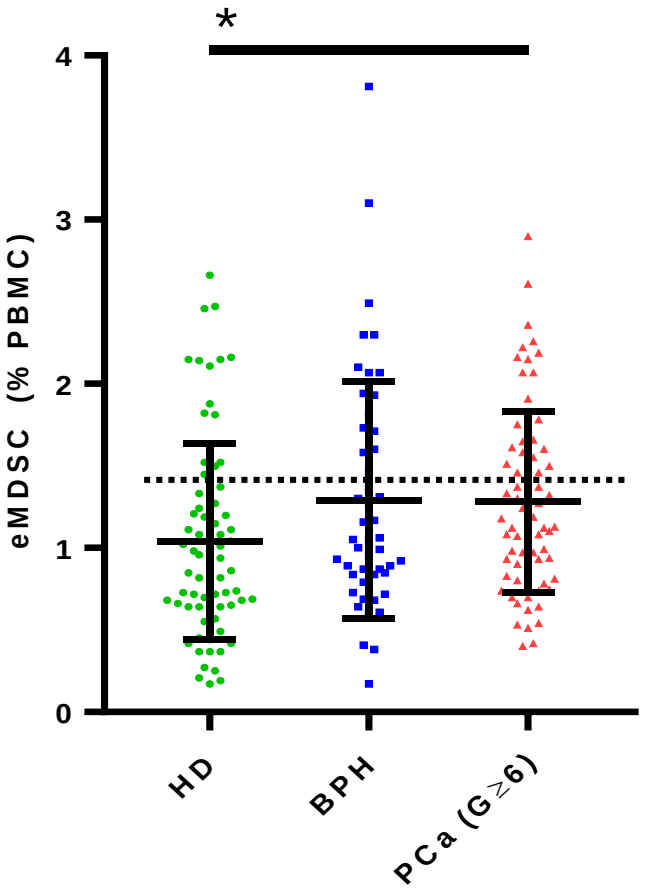
CD3	PE-Vio770
CD4	PE
CD8	APC-Vio770
CD19	APC
CD56	VioBright 515
Live/Dead	DAPI

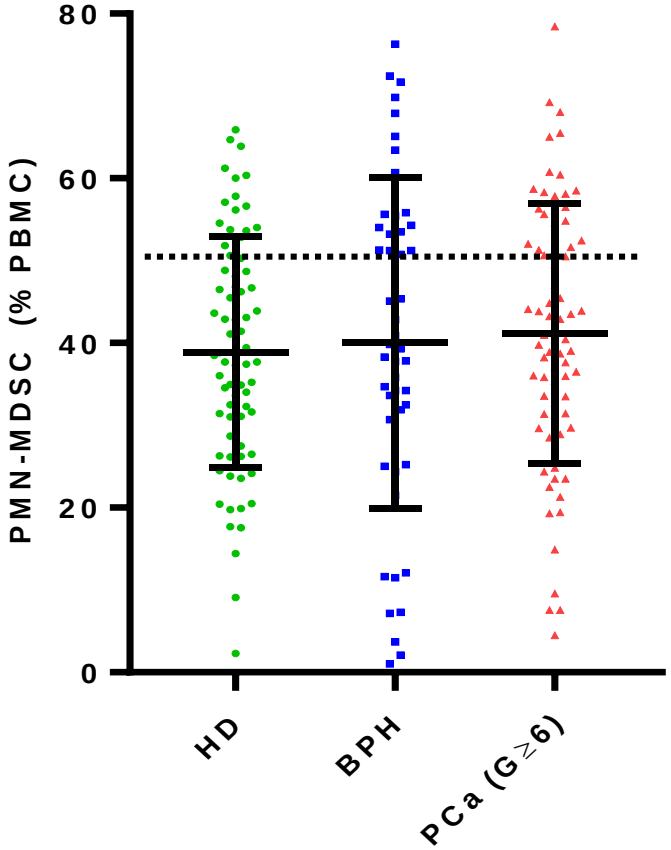
Clinical Characteristics and Categorization

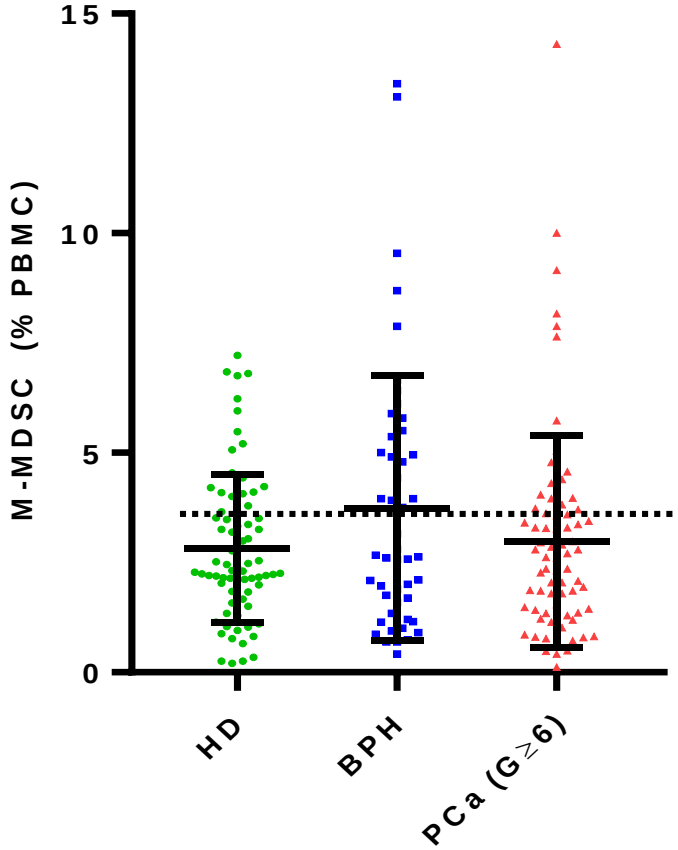
- Prospective blood collection – processed within 20 to 30 hours
- All subjects were already scheduled to undergo a transrectal ultrasound guided prostate (TRUSP) biopsy
- Subjects not included if they had:
  - previous history of cancer (excluding active surveillance)
  - any previous medical intervention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







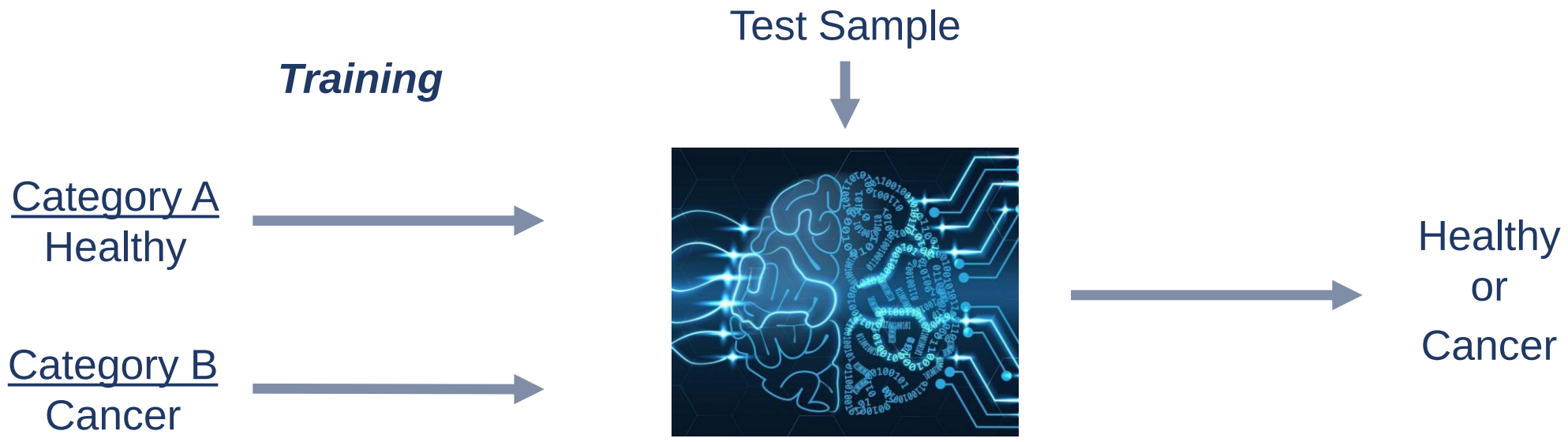
Simple cell counts can provide information about trends, but can only categorize some subjects

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

Healthy Donor (HD) n = 73
Benign Prostatic Hyperplasia (BPH) n = 48
Prostate Cancer (PCa) n = 73

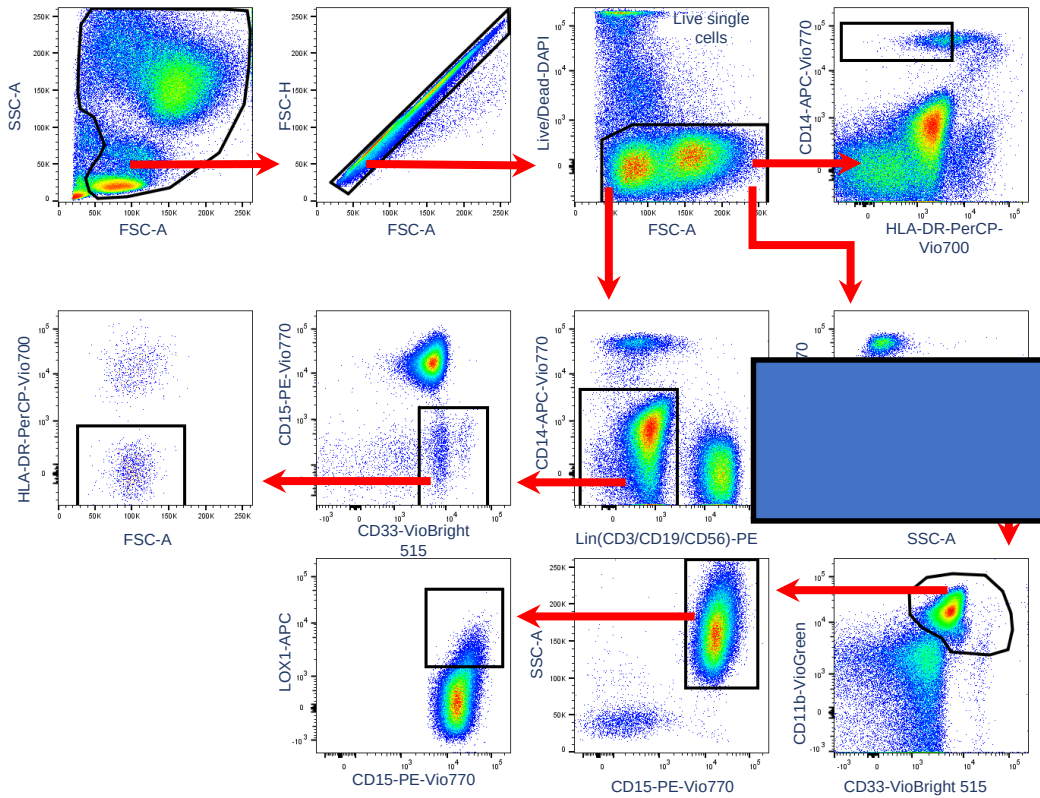
Our Question

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

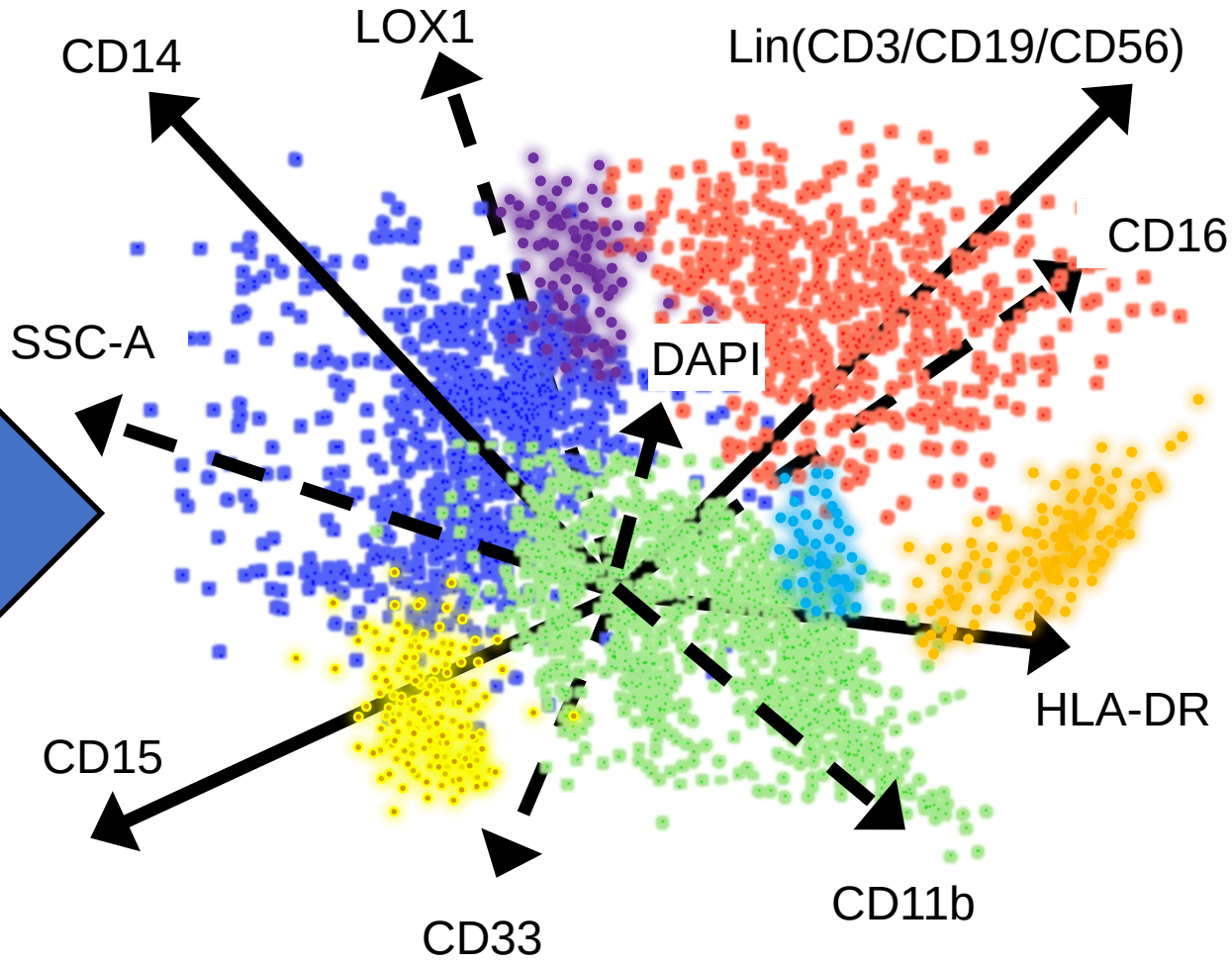


The Inputs – Event Counts

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



Multidimensional Space

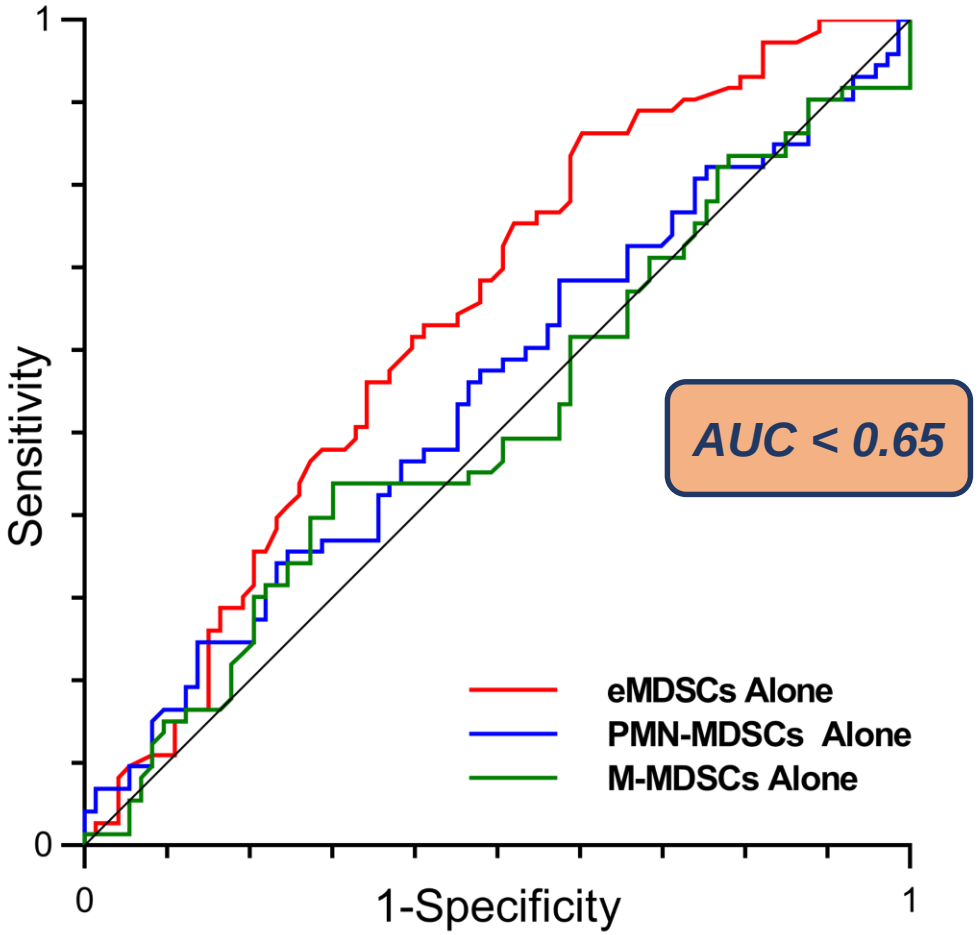


The Neural Network does not see gates, markers, or fluorophores – it just sees numbers

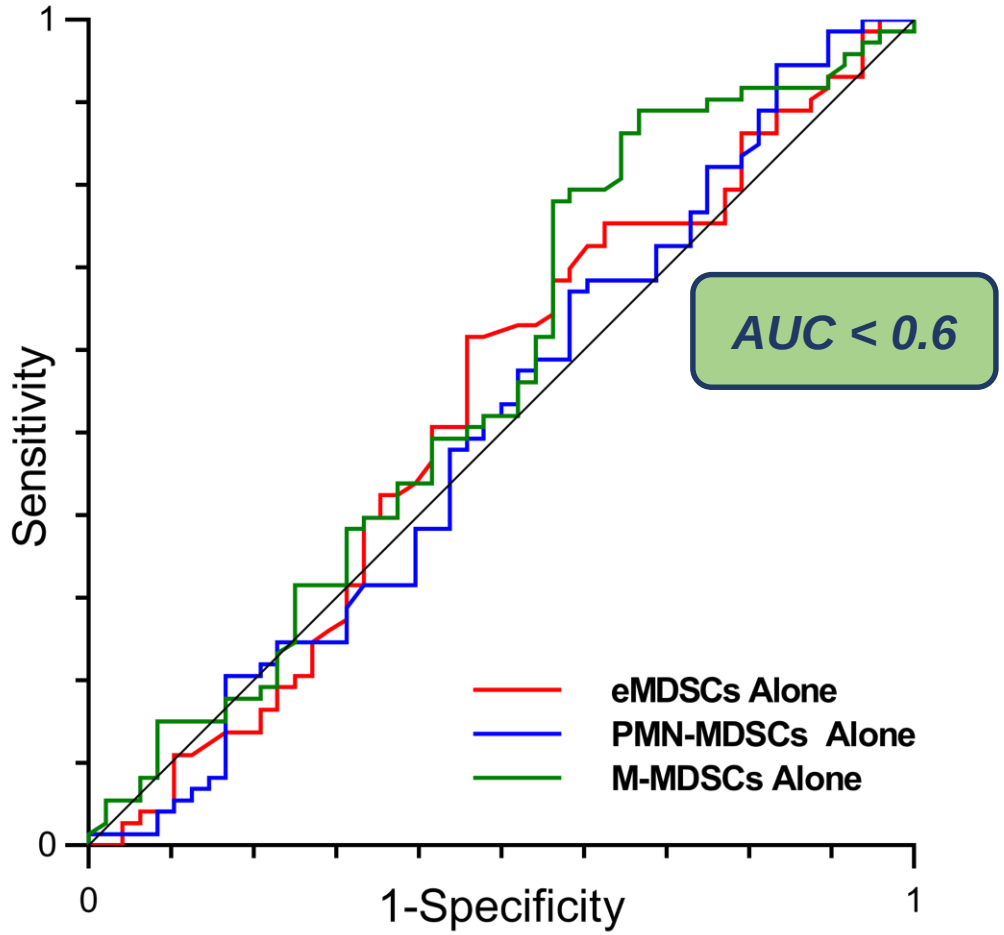
Manual Gating – not enough…

*PCa (Adenocarcinoma) = Gleason ≥ 6

Healthy Donor vs Prostate Cancer



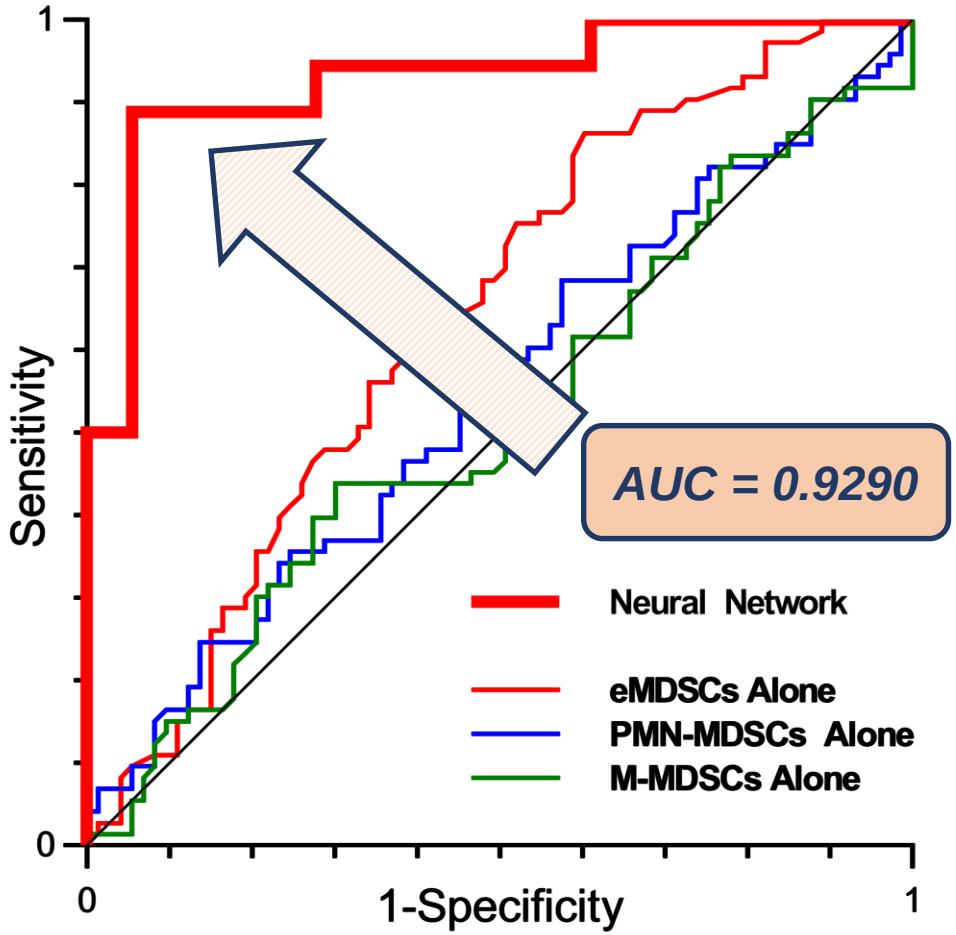
BPH vs Prostate Cancer



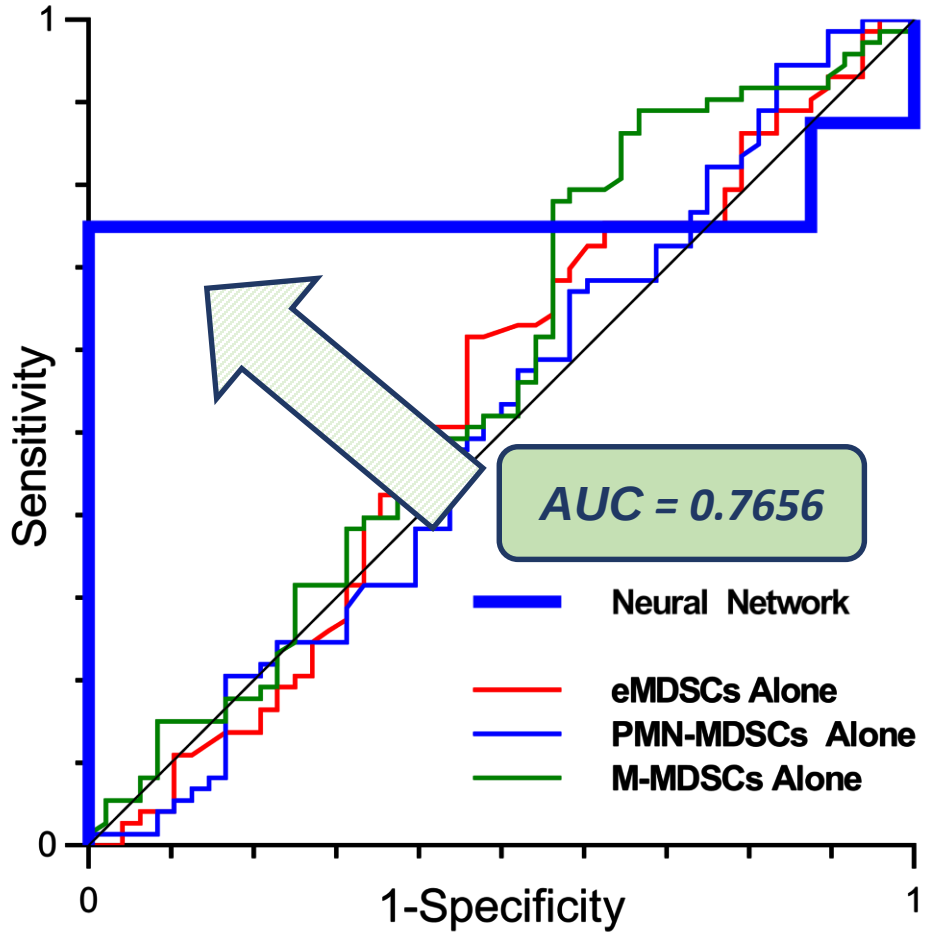
Manual Gating – not enough…

*PCa (Adenocarcinoma) = Gleason ≥ 6

Healthy Donor vs Prostate Cancer



BPH vs Prostate Cancer



What is a clinical application of this technology?

Clinical Application: Confirmatory Testing

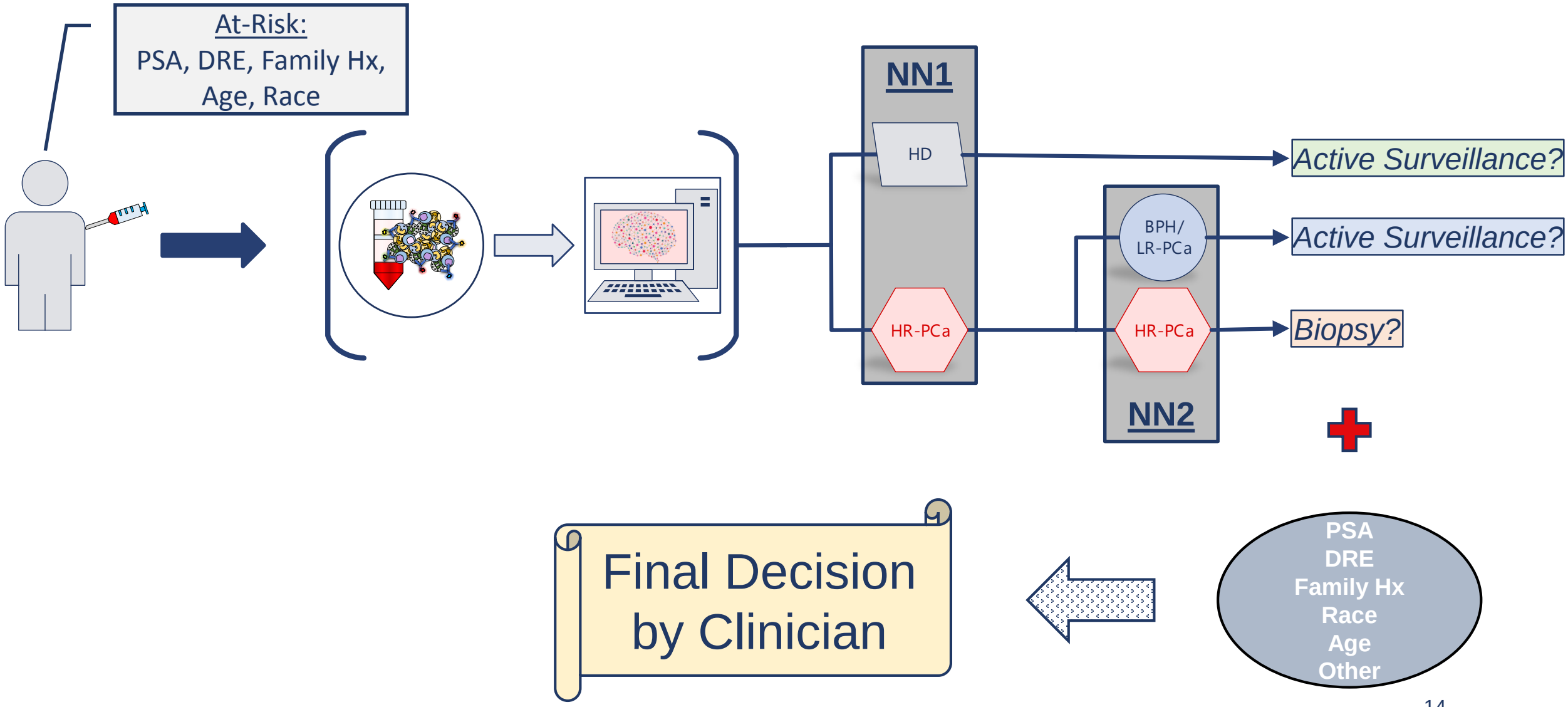
- PSA is not reliable (large numbers of false positives)
- Majority of biopsies are negative
- 20% to 50% of men diagnosed through screening may be over diagnosed
- Gold Standard for Confirming → Prostate Biopsy (invasive/stressful)

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

Source: US Preventive Services Task Force. Screening for Prostate Cancer: US Preventive Services Task Force Recommendation Statement. *JAMA.* 2018, 319(18):1901-1913.

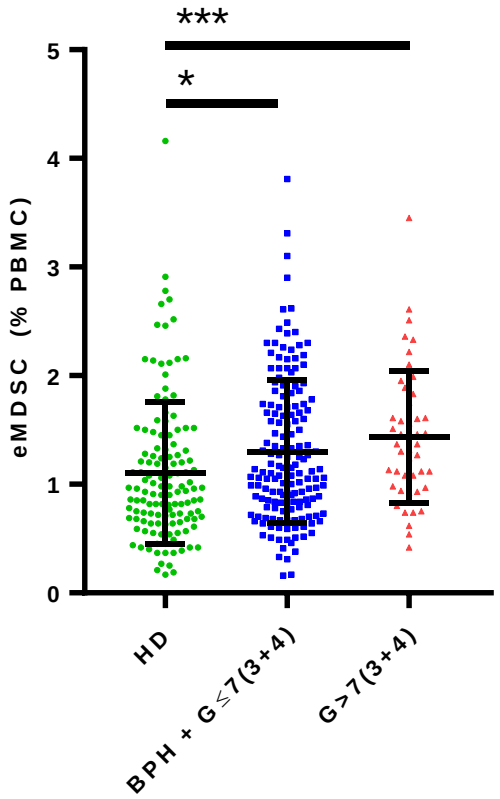
Clinical Application: Confirmatory Testing for PCa Bx

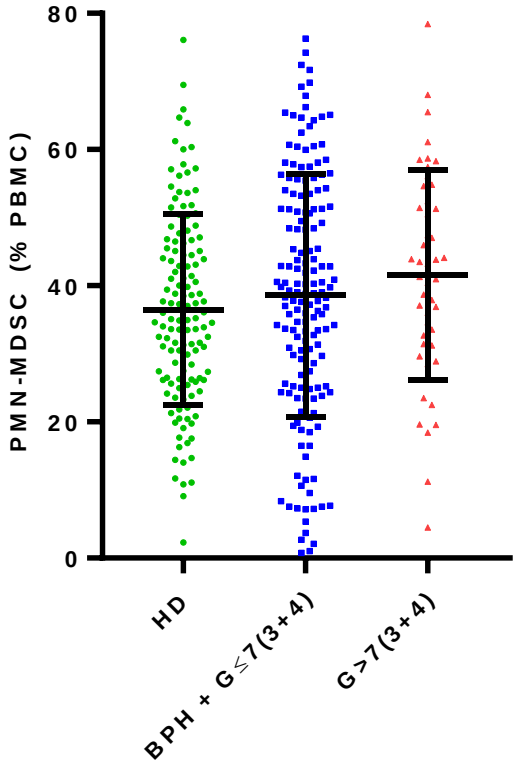


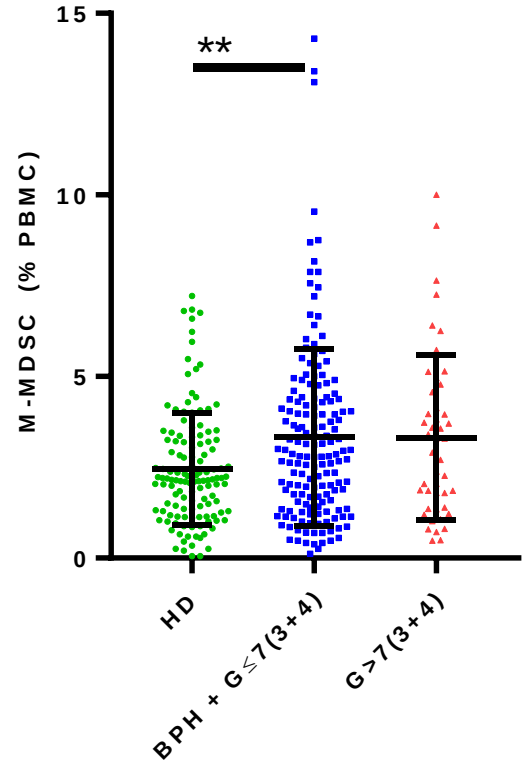
Clinical Characteristics and Manual Counting

- 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

Gleason ≥ 7(4+3)

Gleason ≤ 7(3+4) + BPH

		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	

- 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 cytometry 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.