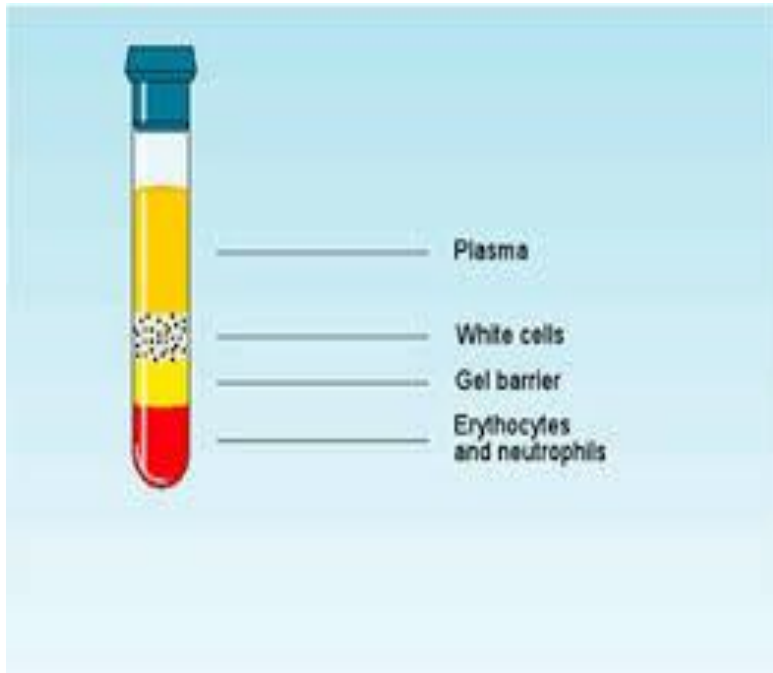




## **A Blood-based Multi-gene Expression Classifier to Distinguish Benign from Malignant Nodules**

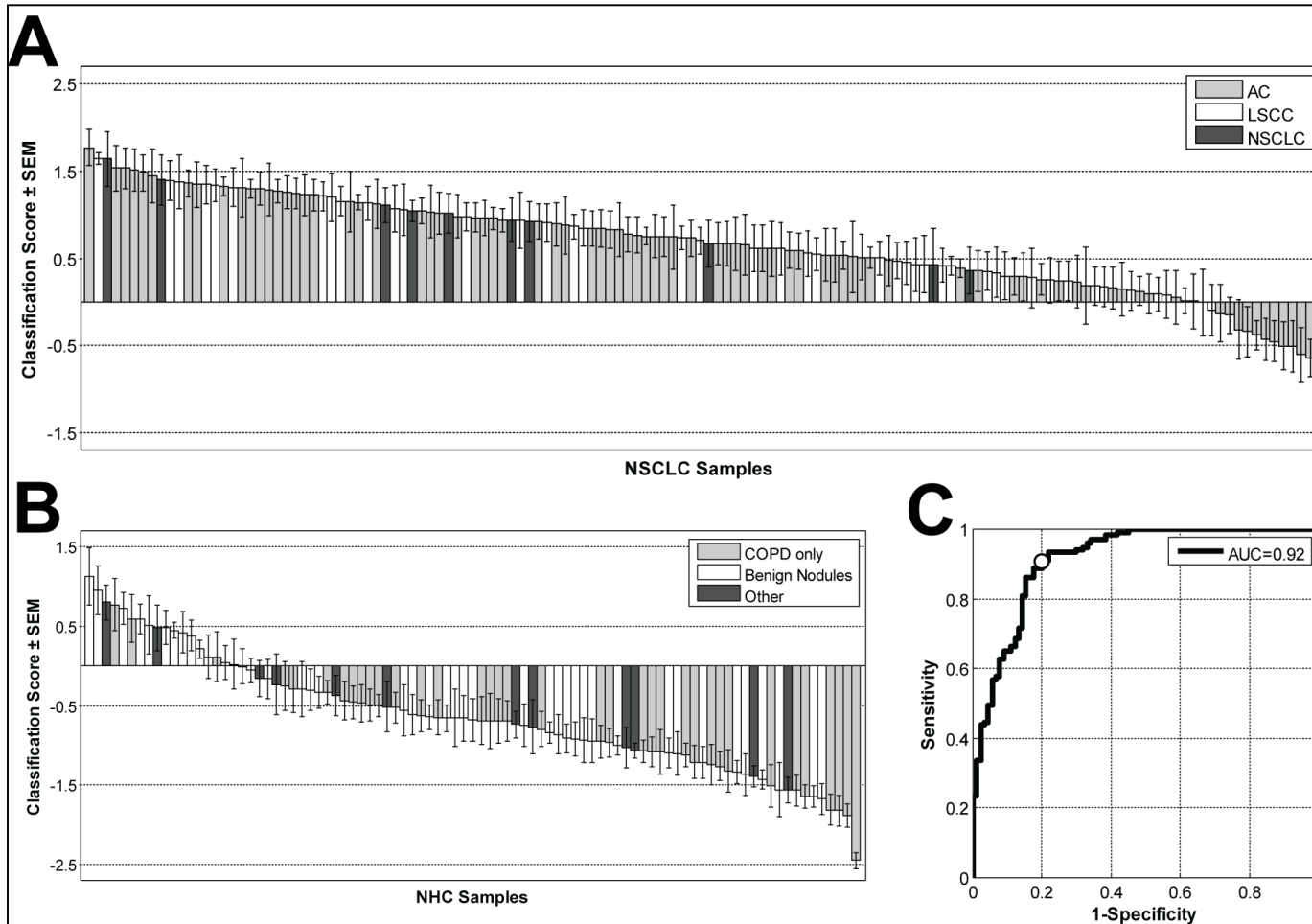
A. Vachani, M. Atalay, R. Bremner, B. Broussard, K. Copeland, K.V. Egressy, J.S. Ferguson, L. Friedman, R.J. Harris, J. Leach, P. McQuary, T. O'Brien, S. Sarkar, N. Sheibani, J. Shuff, T. Siler, C. Southwell, L. Hesterberg

# Peripheral Blood Genomics for Cancer Detection

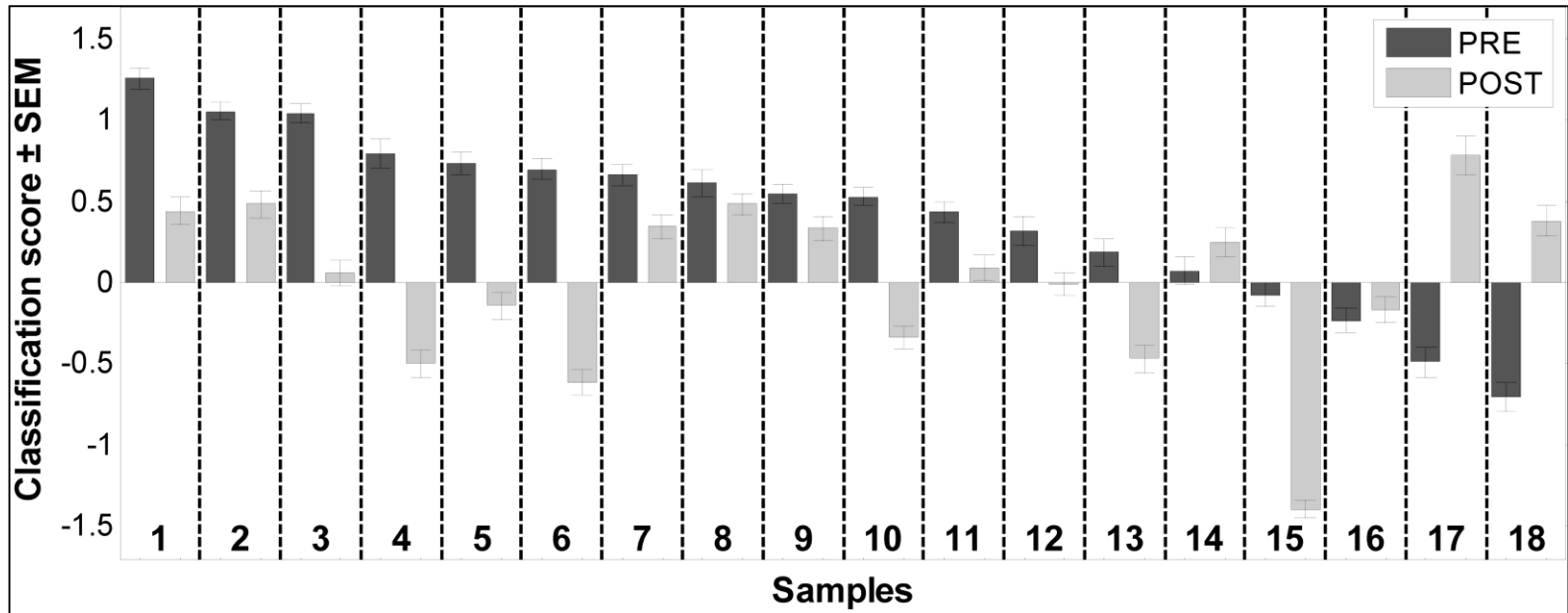


- Original work in CTCL
- PBMCs have altered gene expression due to interaction with tumor
- Solid tumors can have strong effects on T-cell function

# PBMC gene expression distinguishes NSCLC from benign lung disease



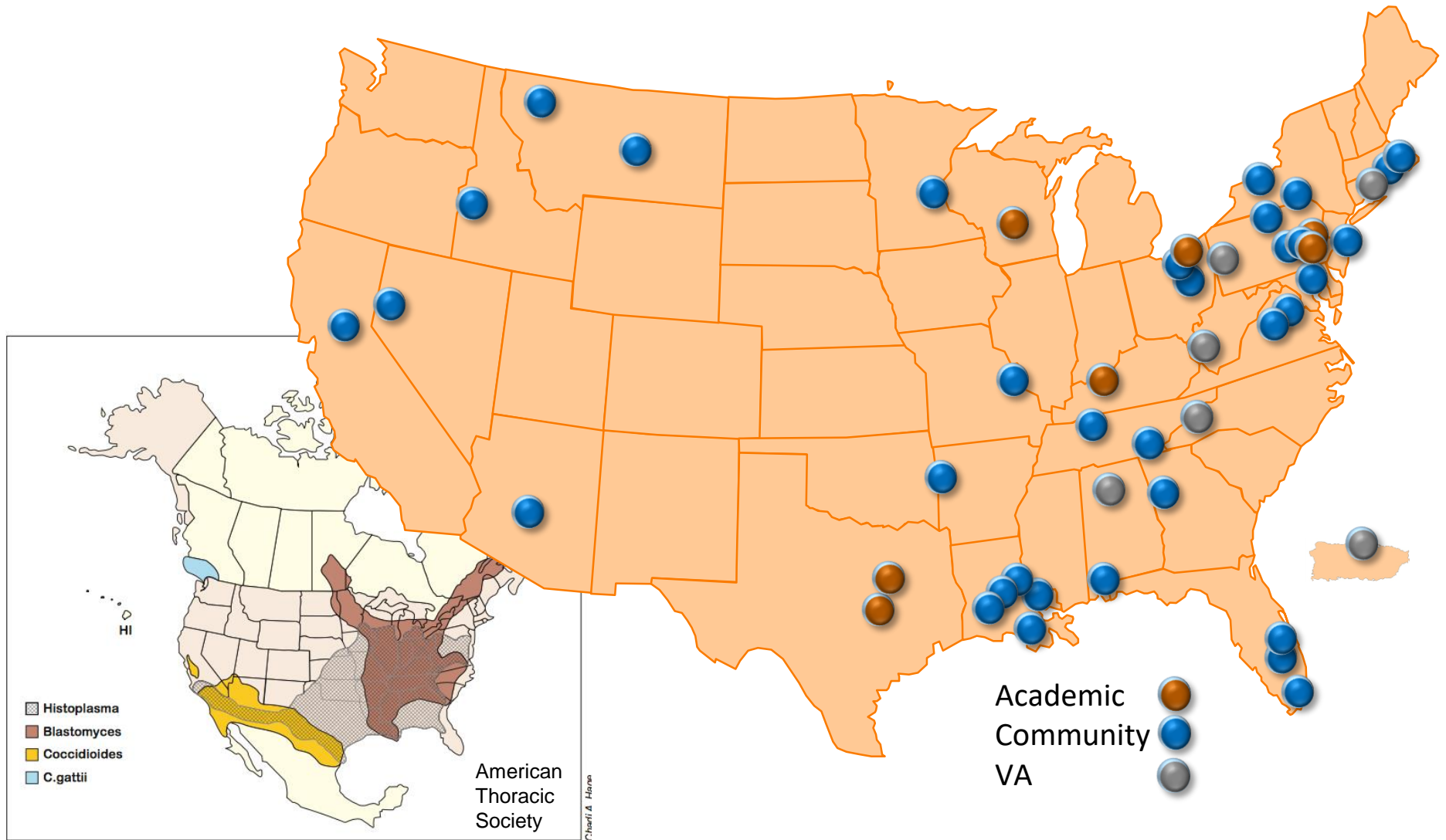
# Effect of tumor removal



# Hypothesis

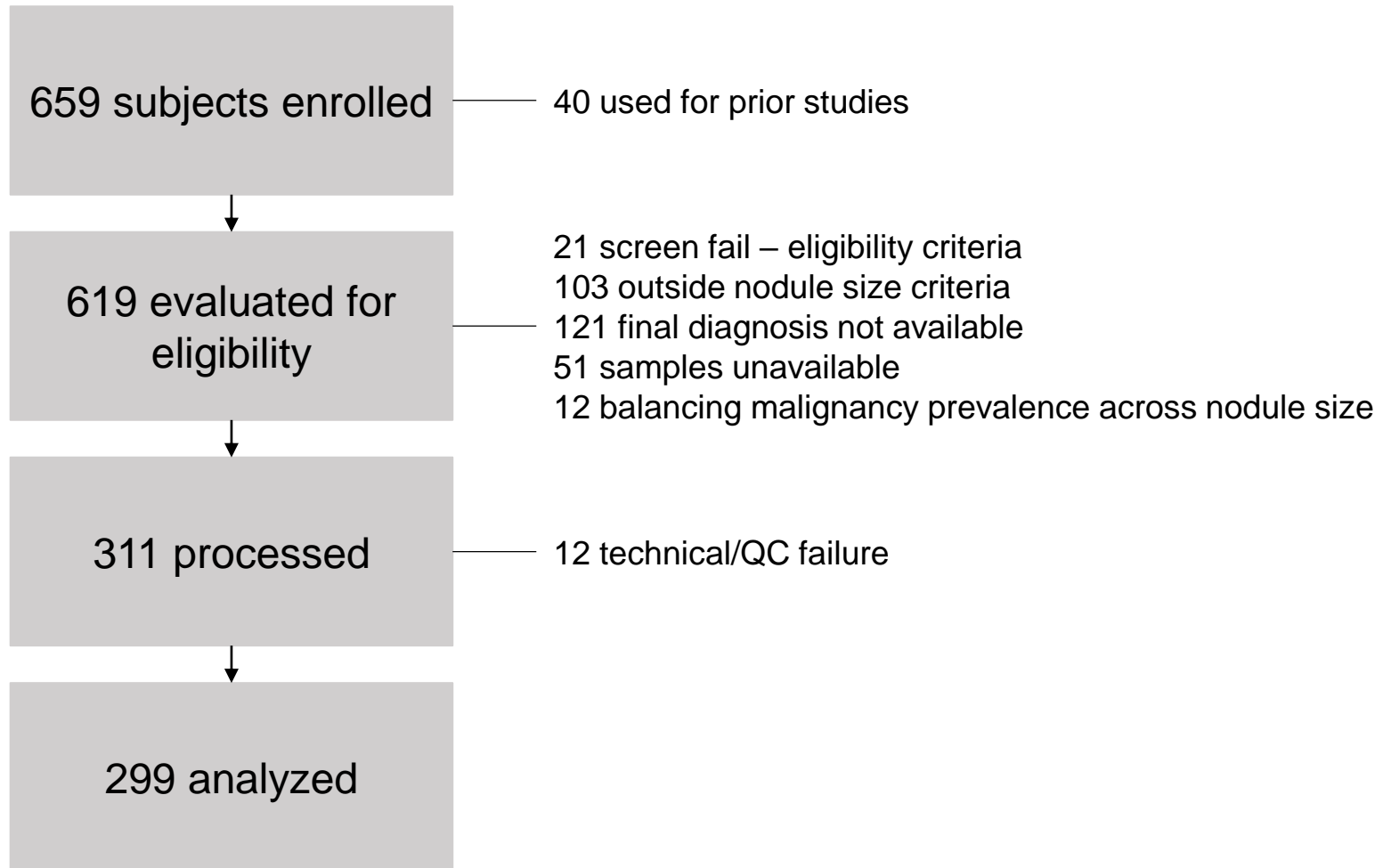
An algorithm can be constructed using gene expression data from whole blood to develop a diagnostic biomarker useful in the management of patients with indeterminate lung nodules

# Multicenter Prospective Observational Study

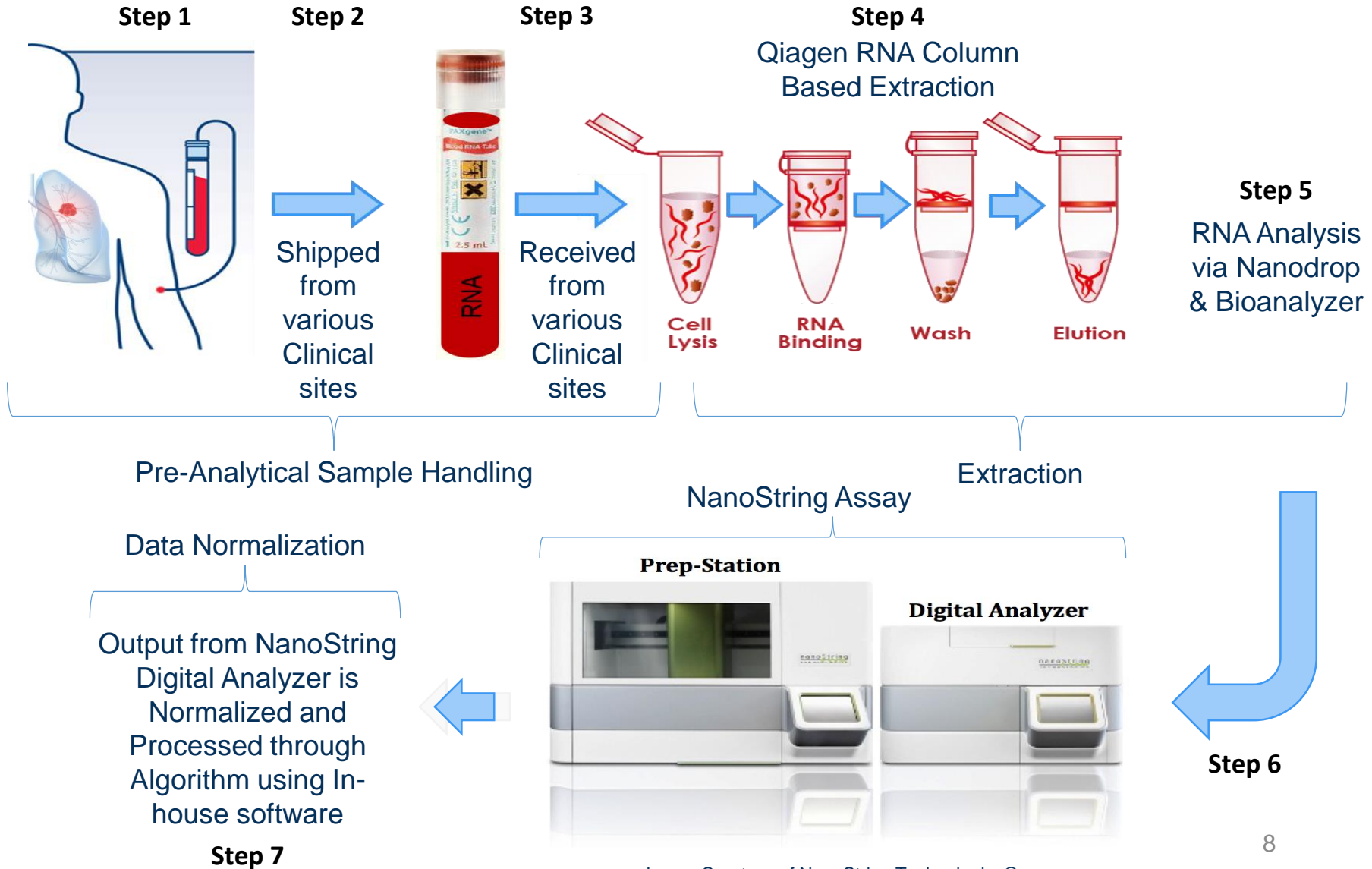


*Histoplasmosis occurs primarily in the areas of the Ohio and Mississippi rivers. Blastomycosis occurs in the central and southeastern United States. Coccidioidomycosis is limited to the southwestern United States. Infection with Cryptococcus gattii occurs in the northwestern United States. The area of histoplasmin skin test positivity in the southwestern United States probably represents cross-reactivity caused by coccidioidomycosis.*

# Cohort Diagram



# Assay Workflow

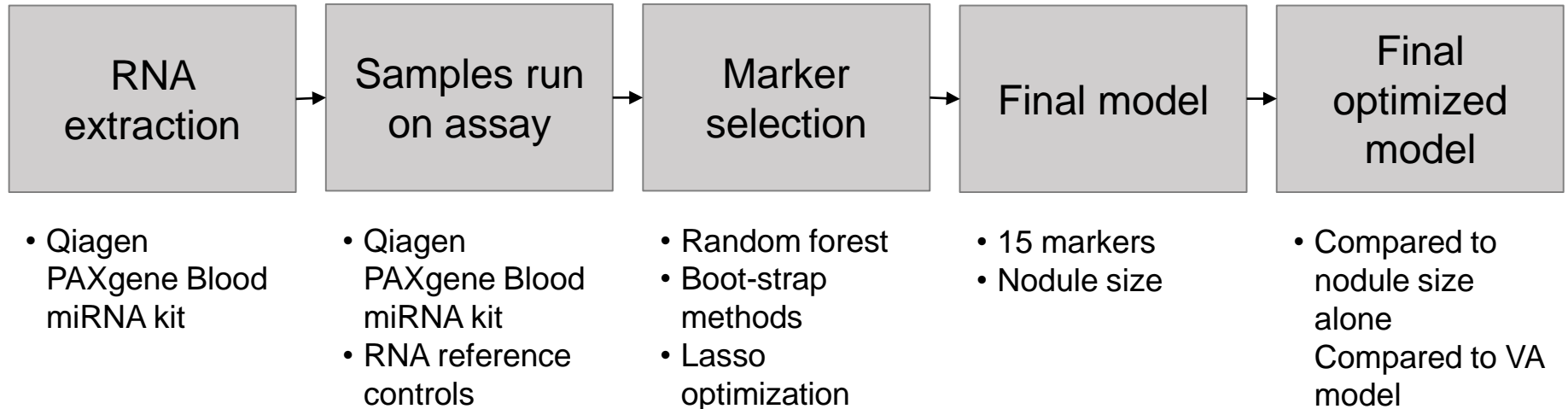




# Baseline Data

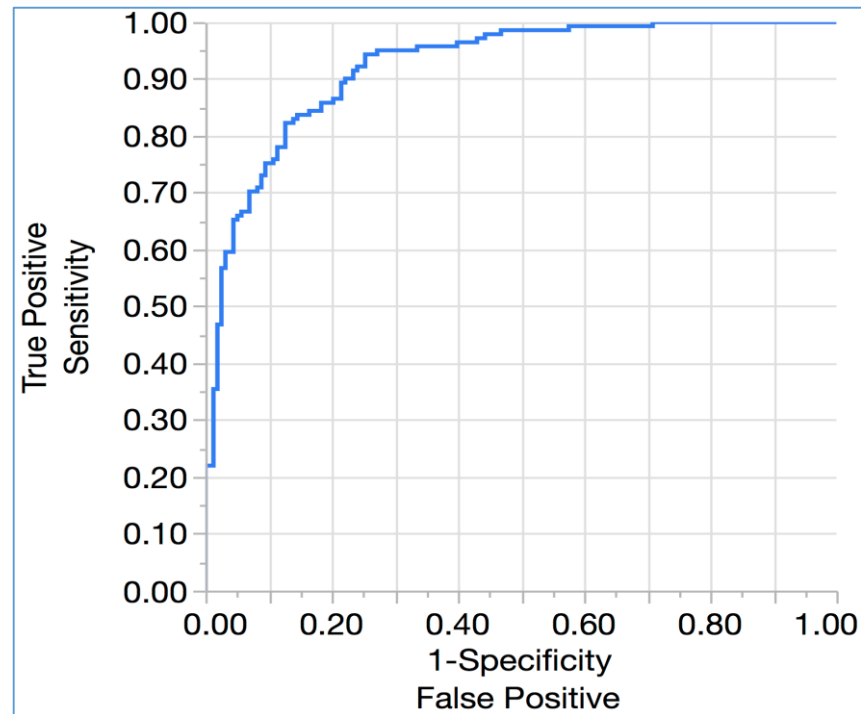
	<b>Benign</b>	<b>Benign %</b>	<b>Malignant</b>	<b>Malignant %</b>	<b>Total</b>
<b>Gender</b>					
<b>Female</b>	84	50%	85	50%	169
<b>Male</b>	74	57%	56	43%	130
<b>Age</b>					
<b>Mean</b>	66.5				
<b>Range</b>	36-89				
<b>Nodule size</b>					
<b>0.5-0.7</b>	63	97%	2	3%	65
<b>0.8-1.0</b>	38	75%	13	25%	51
<b>1.1-2.0</b>	45	38%	74	62%	119
<b>2.1-3.0</b>	12	19%	52	81%	64
<b>Total</b>	<b>158</b>	<b>53%</b>	<b>141</b>	<b>47%</b>	<b>299</b>

# Methods

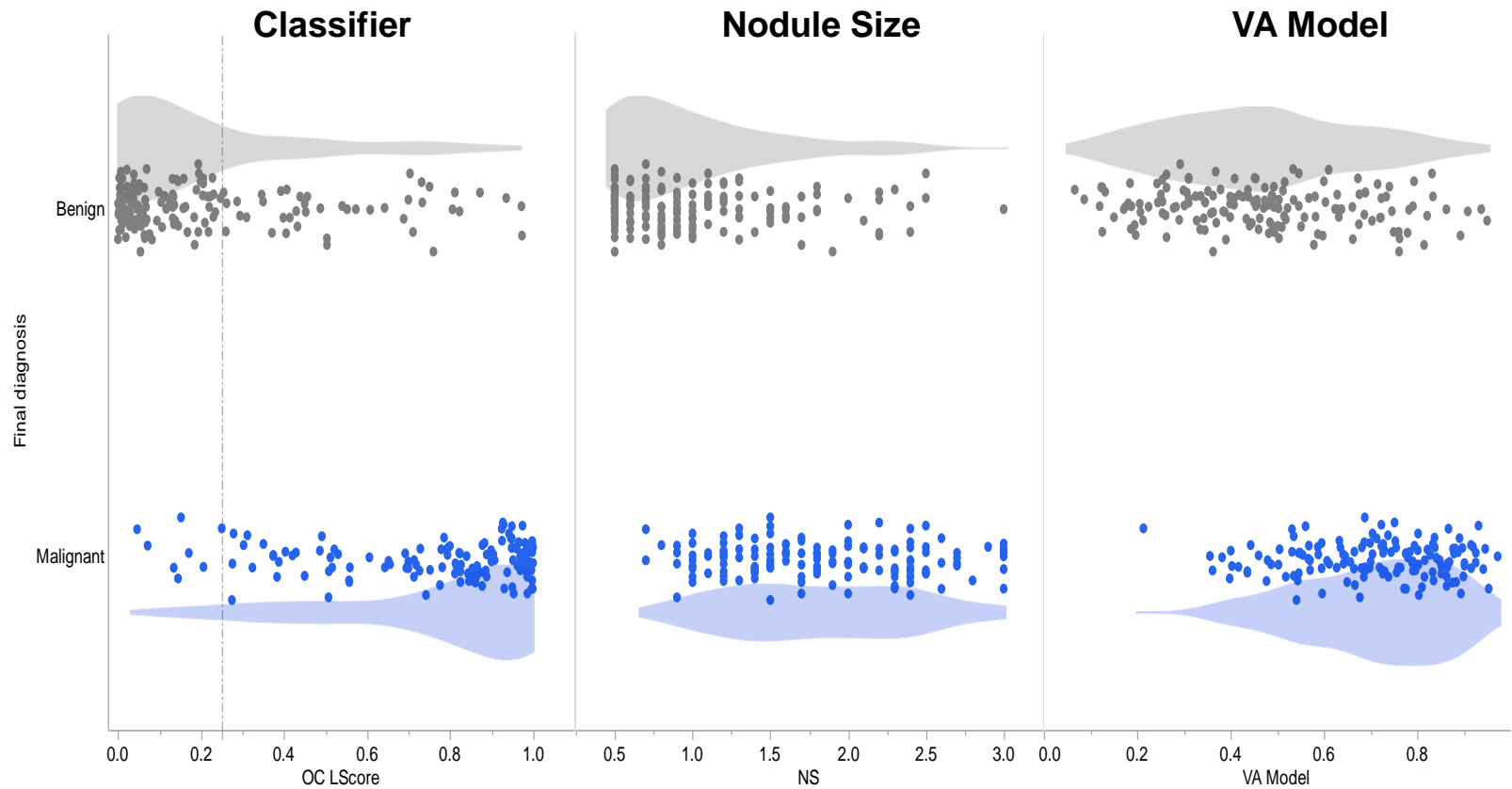


		Final diagnosis		
		Malignant	Benign	Total
Test call	Malignant	134	43	177
	Benign	7	115	122
	Total	141	158	299
Observed sensitivity:		95% (90% - 98%)		
Observed specificity:		73% (65% - 79%)		
Cancer prevalence:		47%		

### Classifier Performance



# Performance Comparison – Nodule Size and VA Model



# Preliminary Conclusions

- Blood based RNA gene expression classifier may allow for a classifier with high sensitivity and a favorable specificity
- Accuracy appears improved compared to nodule size alone or VA model
- Classifier uniquely captures immune response to cancer