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PRECISION MEDICINE WORLD CONFERENCE 2024

Translating Tissue-based Assays into Liquid Biopsies: The Final Frontier for mRNA Assays

Mark Kidd, PhD, Scientific and Laboratory Director

January 24, 2024

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Disclosures

Laboratory and Scientific Director
of Wren Laboratories
Patent holder (NETest, PPQ)

CLIA-certified and CAP-accredited liquid biopsy-focused molecular diagnostic laboratory in Branford, CT

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Tissue-based Assays vs Liquid Biopsies

Conventional Biopsy

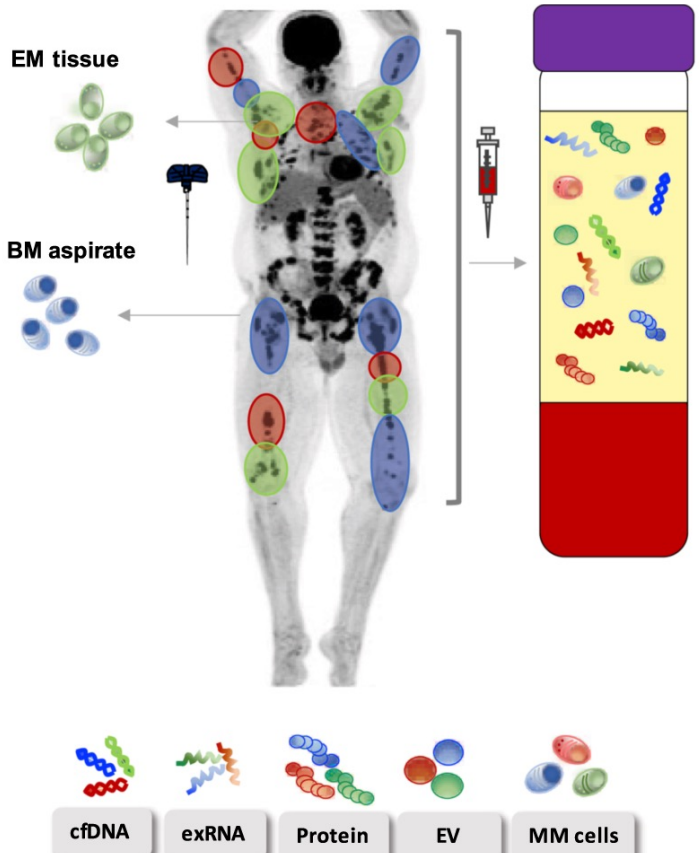
Invasive

Often unsuccessful

Limited snapshot of the tumor

No real-time evaluation

Difficult/tedious



Multiple Myeloma

Liquid Biopsy

Non-Invasive

Easy to do/successful

Comprehensive tumor evaluation

Therapeutic monitoring

Scalable

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Leukemia 2021; 35:2771–2783

Why Liquid Biopsy?

Traditional surgical pathology specimens (biopsies)

- Provide a snapshot of a dynamic process
- Are inadequate for monitoring
- Cannot provide necessary information to guide decision making

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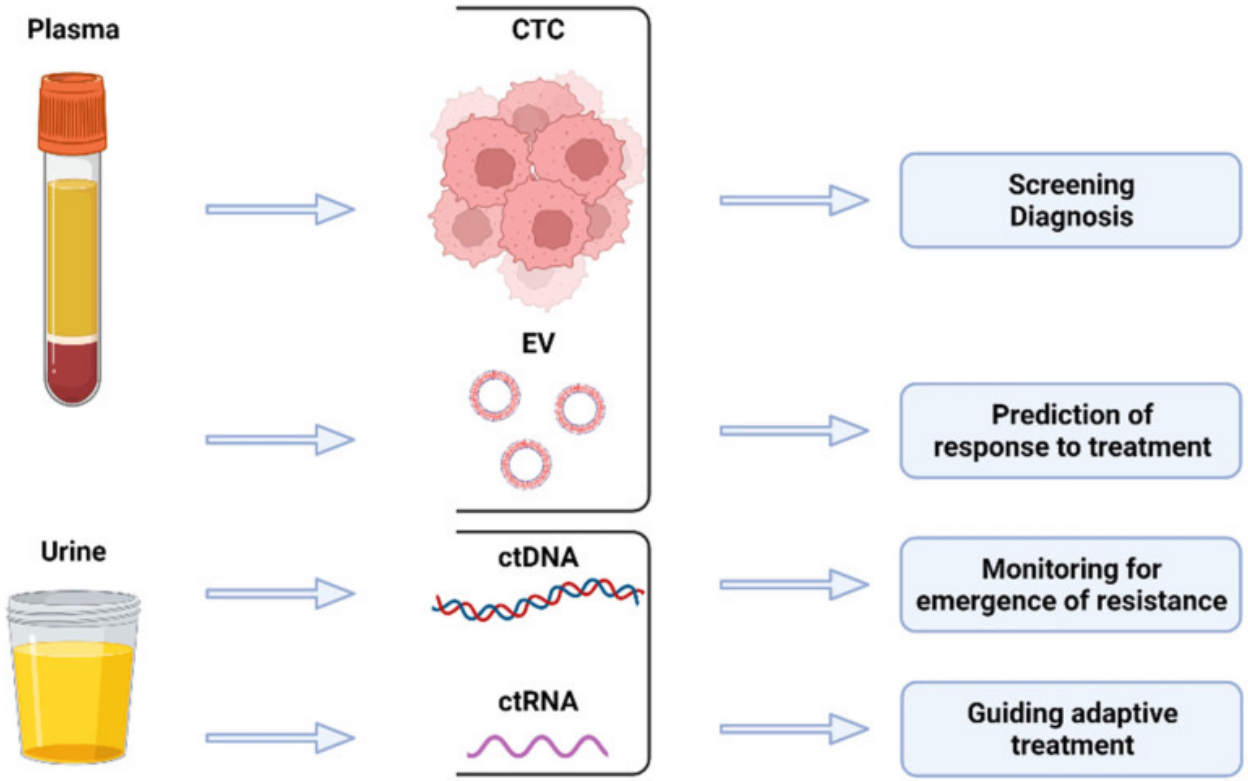
Liquid Biopsy Applications: Prostate Cancer



Circulating tumor cells (CTCs) and extracellular vesicles (EVs), circulating cell-free tumor DNA (ctDNA) and RNA (ctRNA) all provide molecular information to characterize tumors.

Liquid biopsy is a promising minimally invasive tool for PCa management

Cancers (Basel) 2022; 14:1728

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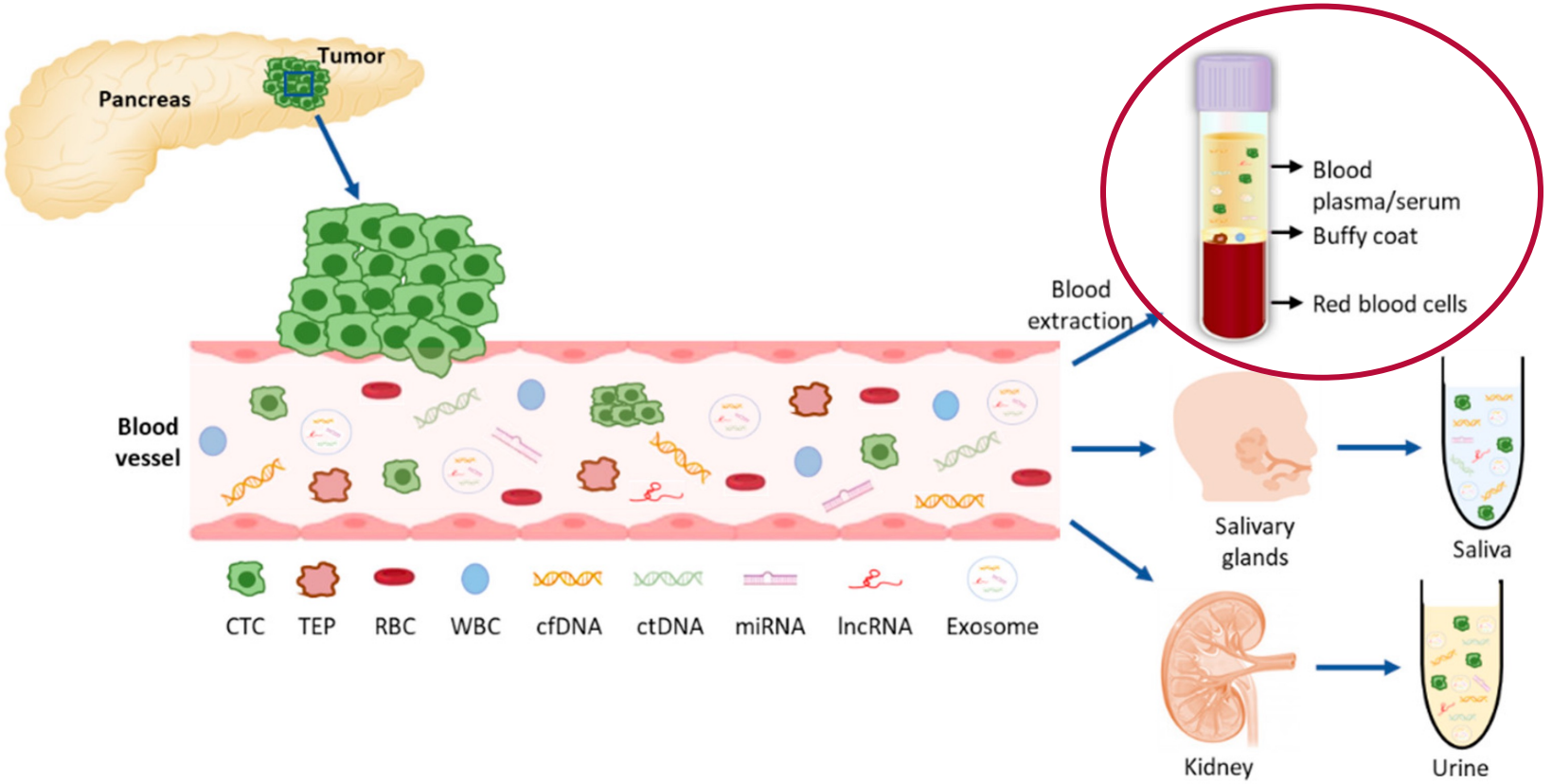
Testing Compartment and Targets



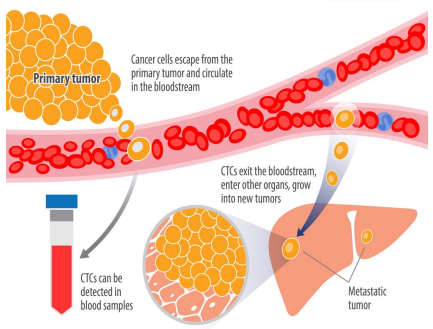
CTC: circulating tumor cell
TEP: tumor educated platelet
RBC: red blood cell
WBC: white blood cell
cfDNA: circulating free DNA
ctDNA: circulating tumor DNA
miRNA: microRNA
lncRNA: long non-coding RNA
Exosome

Minimally invasive, risk-free procedure to detect the presence of genetic material from the tumor in blood and other bodily fluids, providing molecular information that reflects the global status of the disease.

Soto *et al*. Cancers 2021

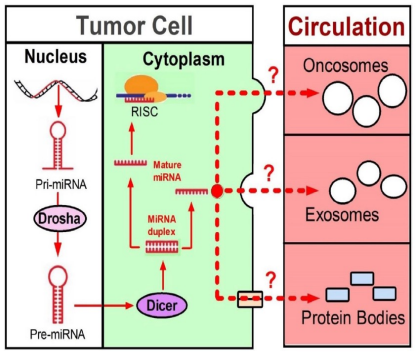
Advantages and Disadvantages

CTCs



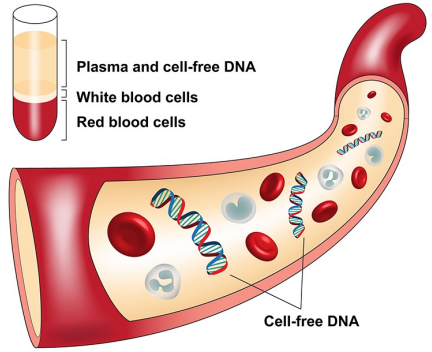
Specific
Single sub-population
Limited numbers
Variable purity
Technology evolving
Limited clinical utility

miRNA/exosomes



Specific
Variable sensitivity
Contamination
Sample yield?
NGS expensive
Technology evolving

cf/ctDNA



Specific
Variable sensitivity
Point mutations
Sample yield?
NGS expensive
Technology evolving

All applications require significant pre-analytic processing

Collection, storage and transportation

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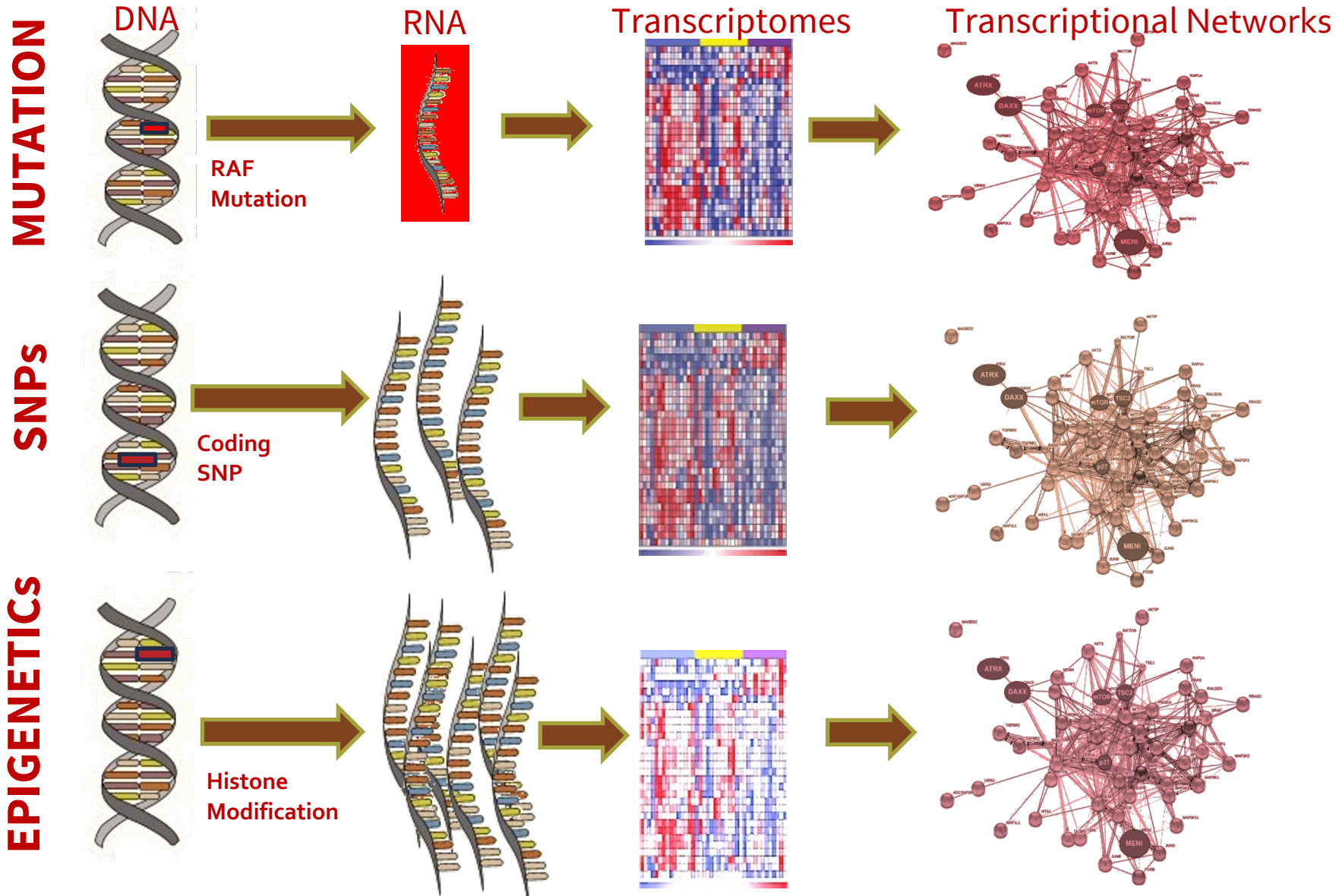
Molecular Targeting



mRNA is the common target

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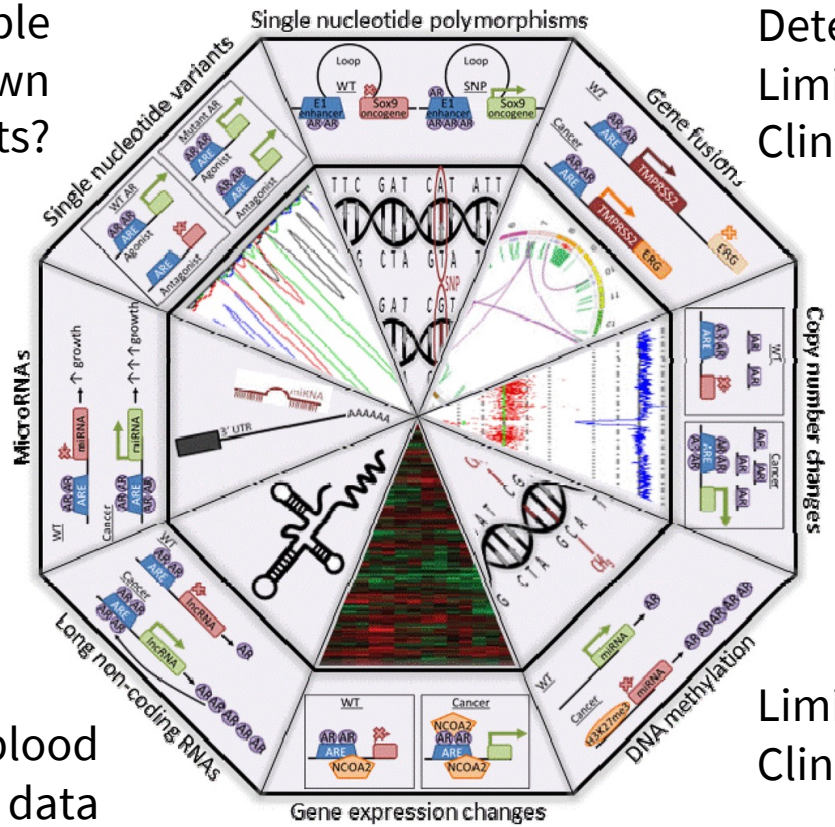
RNA

Multiple
Clinically useful?

Multiple
Significance unknown
Druggable targets?

Detectable in blood
Limited data
Clinically useful?



Detectable in blood
Informative
Pathway activation/
classification
Clinically useful?

Limited data
Clinically useful?

Detectable in blood
Limited data
Clinically useful?

Limited data
Clinically useful?

- **Detectable in blood**
- **Informative – cancer hallmarks**
- **Druggable targets**
- **Classification Marker of tumor behavior**

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mRNA Signatures

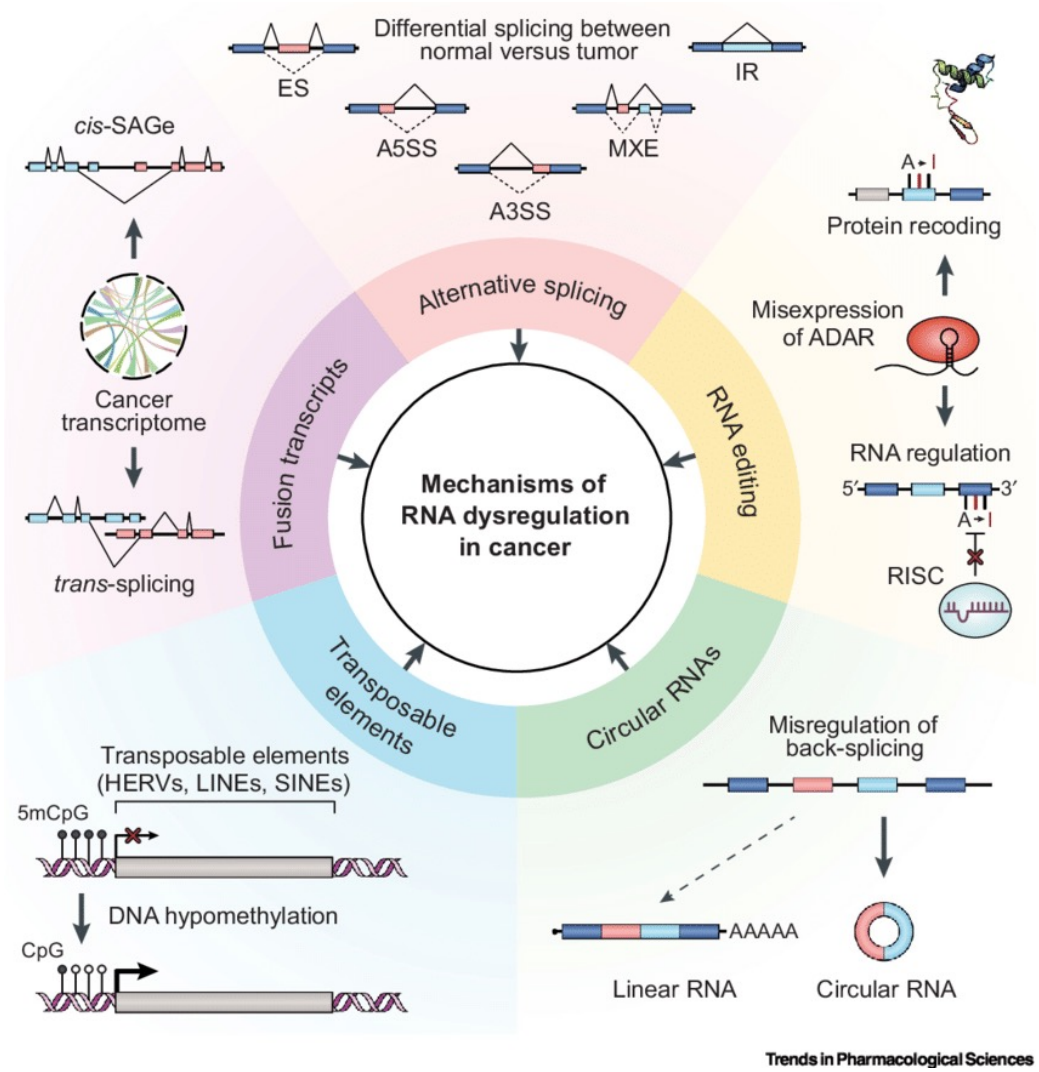
- Messenger RNA (mRNA) – transfers messages from DNA
- The mRNA signature of a cell - transcriptome
- Any alternation in DNA (mutations, copy number changes, epigenetic modifications) or any alterations in RNA regulation (splicing, editing) – changes the transcriptome/signature

Cancer transcriptomes exhibit RNA dysregulation

mRNA is a surrogate marker of DNA status

mRNA can be used to identify tumors/tumor status

Molecular tumor landscape



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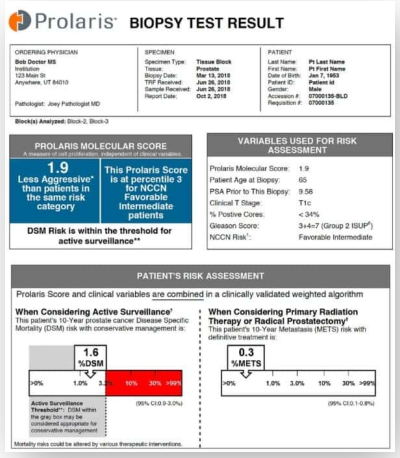
Tissue RNA Biomarker Tools: Prostate Cancer

Prolaris®



Progression (46)

European Urology. 2014;66(3):550-60

oncotype DX®
Genomic Prostate Score

Tx vs. AS (21)

Lancet Oncol. 2011;12:245-55

ConfirmMDx

Repeat Biopsy? (DNA-me)

International J Molecular sciences. 2019;20(8)

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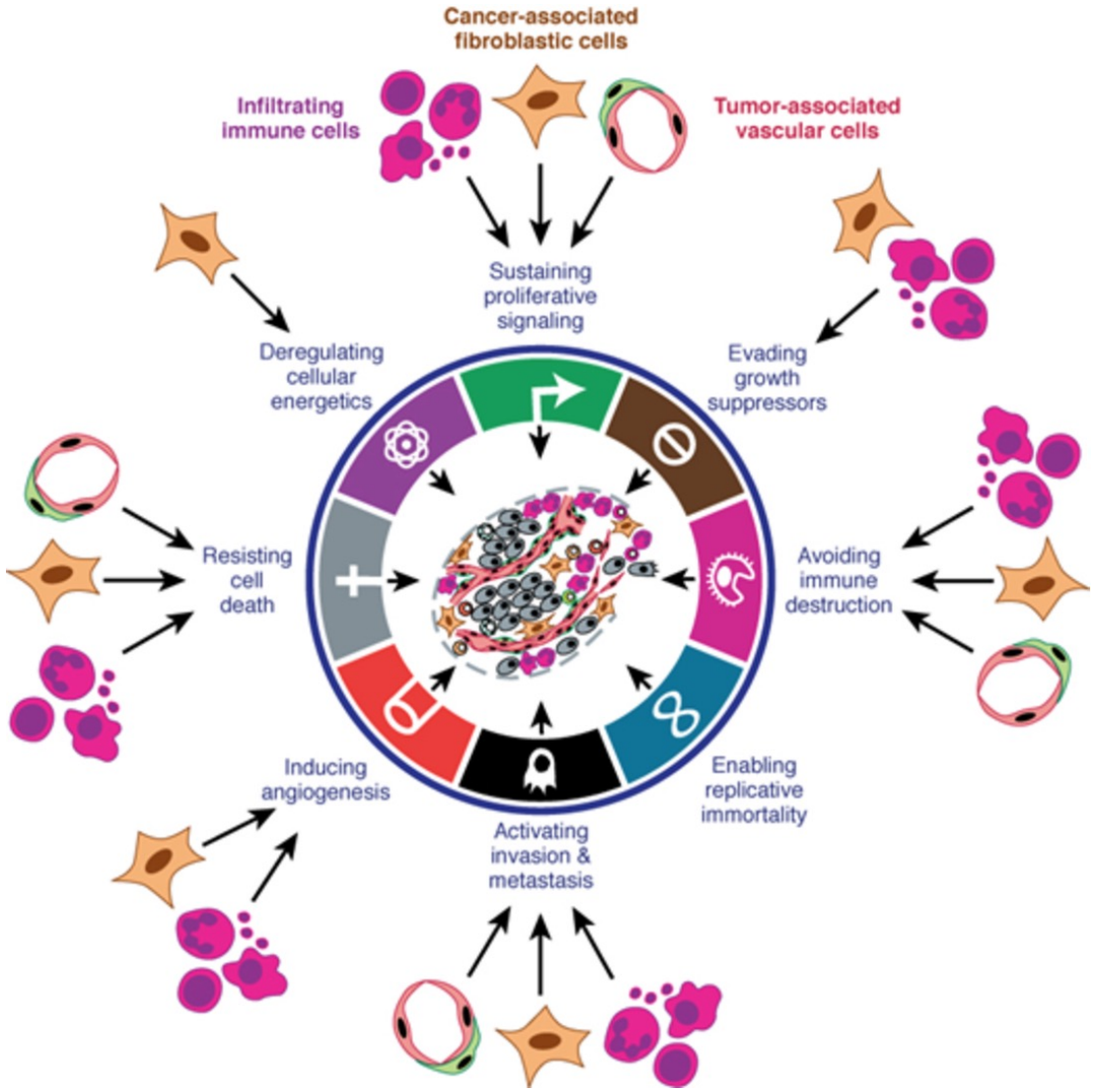
Tumor Message is more than Tissue



The tumor journey reflects the interaction of the genetic make-up of the lesion and the microenvironment as well as systemic responses associated with anti-neoplastic immune activity.

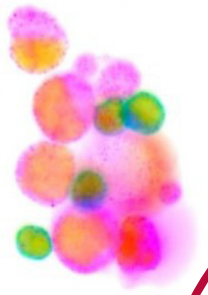
How do we capture the message from the tumor?

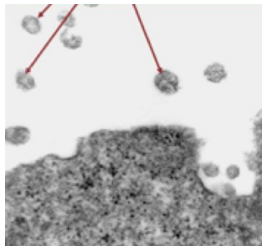
Hanahan D. *Cancer Discov* (2022) 12 (1): 31–46.

Blood Testing Compartment

Circulating Tumor Cells

0+/10ml



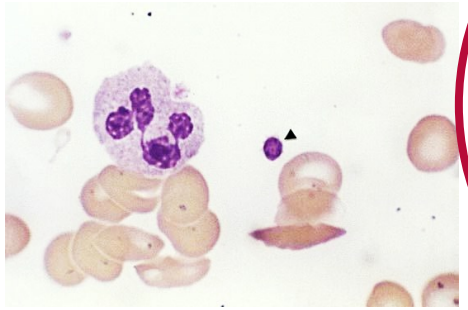


Tumor Exosomes

10^{10}-10^{12}/10ml

Tumor-Educated Platelets

10^{7}/10ml

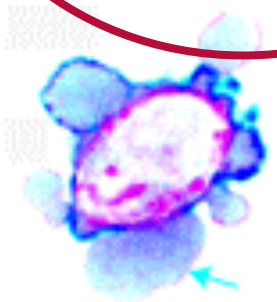


Circulating Nucleic Acids

pg-ng/10ml

"Oncosomes"

100+ /10ml



Utilize the whole blood.

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Molecular/Signature recognition

Identifying (or recognizing) the message (mRNA)

1

What is the message in the tumor cell?

How do we measure tumor mRNA?

2

Can we measure the tumor message outside the cell?

Can the tumor message be detected in blood?

3

Can we build an effective assay to detect this message?

Methodology

Transcriptomes
(RNAseq/microarrays)

↓

***In silico* analyses**
(differentially regulated genes/biologically relevant pathways)

↓

Candidate biomarkers

↓

Assay establishment
(Biomarker finalization/ Modeling/algorithms)
Venipuncture (1ml)

→

Laboratory assay validation
(CAP/CLIA/NYDOH)

↓

Clinical studies
(Validation/ Clinical utility)

↓

Clinical testing implementation

→

Alternative Testing Compartments
Saliva

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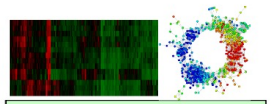
Signature Recognition and Validation

(Prostate Cancer)

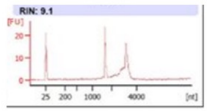


Signature Derivation
1,159 tissue transcriptomes
Network analysis
Functional enrichment
Differential expression

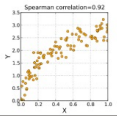
Tumor Specificity
TCGA: *n*=10,990
RNAseq
Heirarchical clustering analysis

Tissue Confirmation
Surgical samples: *n*=50
qPCR
Matched normal tissue vs. tumor samples

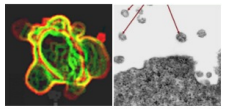
Blood Detection
65 blood samples (con, BPH, PCa)
Targeted RNAseq/ qPCR 27 markers



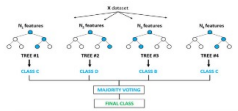
Blood RNA Stability/ Reproducibility
30 controls/30 PCas
RIN/Bioanlyzer
qPCR



Tumor:Blood mRNA Concordance
50 PCas
Matched tumor/ blood qPCR

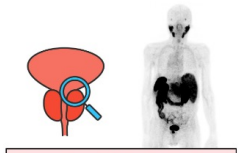


Non-tumor Source Evaluations
Whole blood
Platelets/Tumor blood
Exosomes/EVs/Immune
RNAseq



Blood Algorithm Development
430 age-matched subjects (control, BPH, PCA)
qPCR 27 markers
"PROSTest"

Prospective Validation of Algorithm
Age-matched controls, BPH, PCas: *n*=303
"PROSTest" vs. PSA levels/AUROC



Surgical Validation of Algorithm
Prospective, *n*=47 radical prostatectomies
"PROSTest", PSA and ^{68}Ga-PSMA imaging

1. Identify tumor signature
2. Evaluate gene signature in blood testing compartment
3. Build a qPCR-assay and test algorithm

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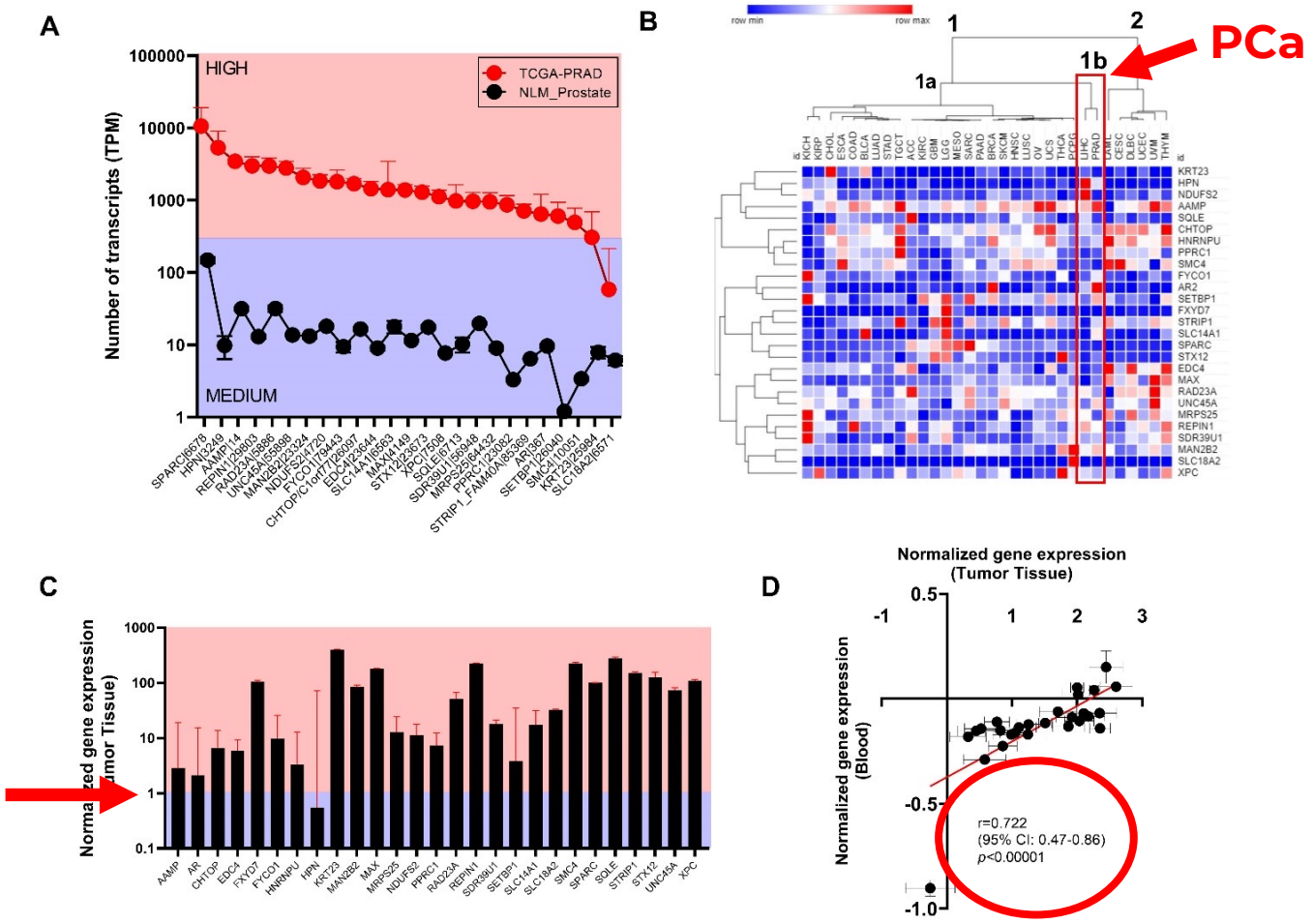
Signature Recognition



A. RNAseq (tumor and normal tissue) TCGA (*n*=494 PCa, *n*=51 normal prostate)

B. Hierarchical clustering – 32 different cancers (*n*=10,990)

C. qPCR PCa tumor tissue (*n*=50)

D. qPCR PCa tumor tissue and blood (matched: *n*=50)

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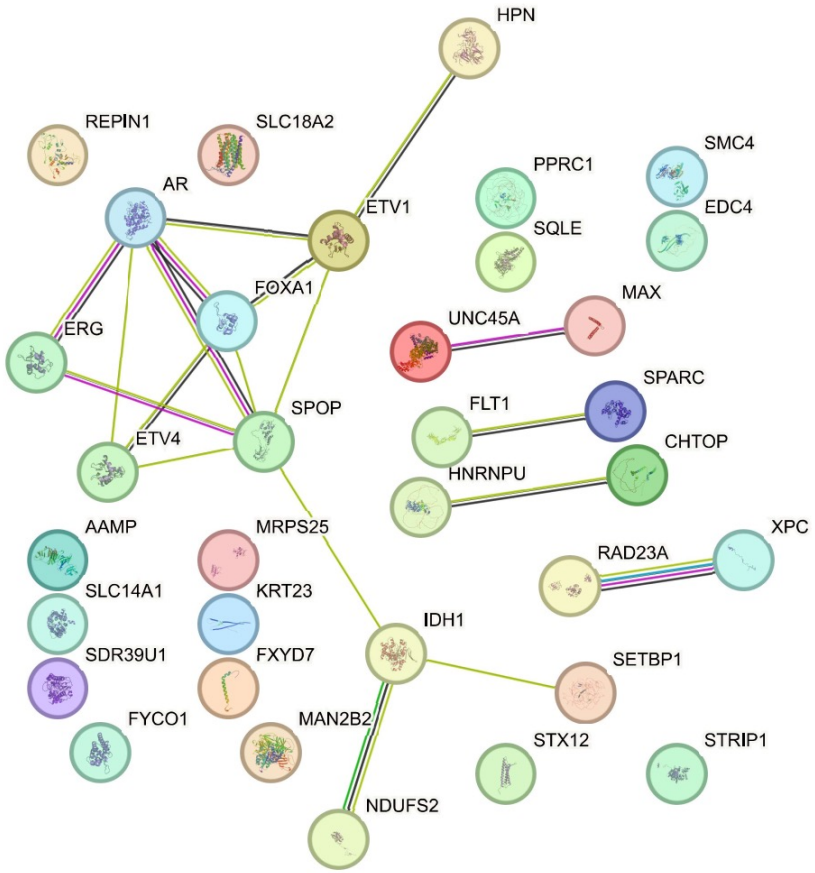
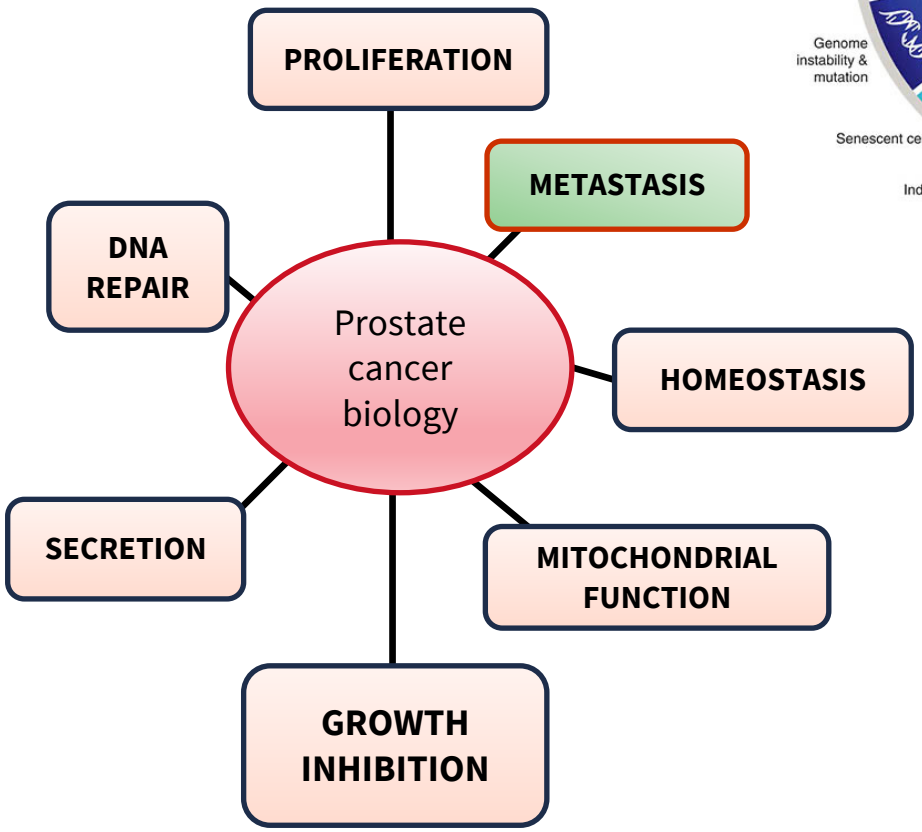
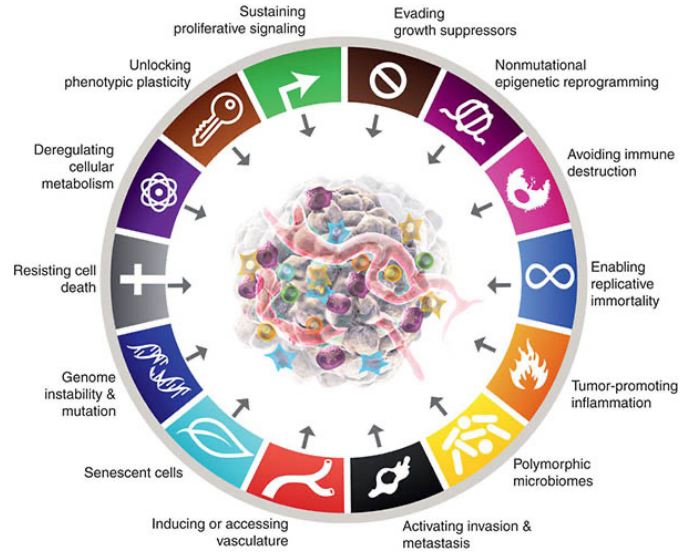
Signature – The PROSTest



PROSTest ™ INTERACTOME



PCa HALLMARKS



String-DB

Target Genes - scRNAseq

#	Symbol	Detected‡	Glandular epithelial			Endothelial	Smooth muscle	Blood, immune and mesenchymal			AR regulated Gene Expression†
			Basal cell	Club cell	Glandular cell			T-cell	Macrophage	Fibroblast	
1	*AAMP*	Yes	43.2	36.2	35.9	28.7	33.5	30.8	21.7	27.7	Yes(-)
2	*AR*	Yes	178.1	80.6	499	140.4	64.5	122.4	18.3	126.7	Yes(+)
3	*CHTOP*	Yes	45.3	37	34.6	49.2	41.4	44	38.3	35.6	Yes(+)
4	*EDC4*	Yes	1.3	0.5	1.9	0.9	0.6	2.6	1.2	0	Yes(+)
5	*FXYD7*	Yes	0.2	0	0	0	0	3.7	0.9	0	Yes(+)
6	*FYCO1*	Yes	9.3	9.6	13	10.3	14.6	13.6	5	12.5	Yes(+)
7	*HNRNPU*	Yes	454.8	284.6	254.9	363.9	360.7	430.9	517.4	405.3	Yes(+)
8	*HPN*	Yes	3.8	0.6	23.4	0.3	1.8	2.3	0.7	1.3	Yes(+)
9	*KRT23*	Yes	77.2	41.4	2.2	19.6	3	2.6	2.9	0.7	No
10	*MAN2B2*	Yes	9.1	16.2	26	8.7	15.8	22	15.2	21.1	Yes(+)
11	*MAX*	Yes	54.4	46.8	64.4	49.8	41.4	73.8	61.2	40.3	Yes(-)
12	*MRPS25*	Yes	35.8	37	68.7	27.2	31	43.9	37.6	25.1	Yes(+)
13	*NDUFS2*	Yes	64.3	54.2	51.6	89.9	82.7	69.3	72.4	71.3	Yes(-)
14	*PPRC1*	Yes	11.7	6.6	5	7.5	5.5	13.1	11.3	5.9	Yes(+)
15	*RAD23A*	Yes	84.8	85.9	77.3	74.3	99.7	87	89.5	55.4	No
16	*REPIN1*	Yes	37.8	29.4	27.4	34.7	23.7	34.6	24.3	18.5	Yes(-)
17	*SDR39U1*	Yes	29.4	23.8	21.5	30.2	27.4	29.5	21.5	24.4	Yes(+)
18	*SETBP1*	Yes	27.9	6.8	20.2	19.3	45	11.5	6.5	63.4	Yes(+)
19	*SLC14A1*	Yes	4.6	104.5	6.3	10.9	2.4	13.3	3.1	21.8	No
20	*SLC18A2*	Yes	0	0	7.2	0.2	0	1.5	0.5	0	No
21	*SMC4*	Yes	39.4	14.3	7.8	34.7	24.3	27.7	32.5	17.2	Yes(-)
22	*SPARC*	Yes	59.9	4.7	0	370.8	225	8.5	5.5	233.7	No
23	*SQLE*	Yes	15.6	26.1	43.3	10.6	9.1	12.4	22.4	7.3	No
24	*STRIP1*	Yes	7.3	6.1	10.7	7.5	2.4	7.5	7	5.3	No
25	*STX12*	Yes	60.1	33.6	103.1	45.3	32.8	70.8	54.8	29	Yes(-)
26	*UNC45A*	Yes	22.1	31.7	28.1	30.2	43.8	24.6	17.8	17.8	No
27	*XPC*	Yes	60.6	40.9	37.8	45.3	35.9	59.9	36.4	43.6	Yes(-)

*mRNA expression detected in single cells

†Protein Atlas single cell evaluation https://www.proteinatlas.org/gene/single+cell+type/prostate nTPM 3

†AR = androgen receptor signaling. Gene expression is regulated by androgen receptor activation (from RNAseq data-evaluation of differential expression following 24 hr incubation with either 10nM dihydrotestosterone [AR- agonist] or 10µM biaclutamine [AR-antagonist] in LNCaP cells. From Shah et al. Oncogene 2020; 39:6172-6189, Supplemental dataset 1) 4. No: no experimental evidence; Yes(+): activated; Yes(-): repressed.

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Immune Cells

#	Symbol	Whole Blood (TPM)*	PBMCs (nTPM)‡	Single cell flow-sorted (nTPM)‡	Role in Hematopoeisis (DMAP)† **	Immune cell specificity and cell distribution‡
1	*AAMP*	0.05	Monocyte (60) B-cell (60)	**ncMonocyte (212) iMonocyte (209) Myeloid DC (192)**	Erythrocyte	Low immune cell specificity
2	*AR*	0.02	DC (40) Platelets (38)	ND	None	Not detected in immune cells
3	*CHTOP*	21.0	T-cell (80) B-cell (74)	Basophil (85)	**B-cell CD4/CD8 Monocyte Neutrophil**	Low immune cell specificity
4	*EDC4*	17.5	NK cell (0.9)	ncMonocyte (11) T-reg cell (11)	**B-cell CD4**	Low immune cell specificity
5	*FXYD7*	2.1	T-cell (16)	NK cell (52)	None	**Immune cell enhanced (NK-cell)**
6	*FYCO1*	2.3	T-cell (14) DC (14)	MAIT T-cell (2.6) GdT-cell (2)	None	Low immune cell specificity
7	*HNRNPU*	33.7	**Macrophage (378) DC (317)**	pDC (31.4) Naïve CD4 (25.5)	**B-cell CD4/CD8 Erythrocyte Neutrophil**	Low immune cell specificity
8	*HPN*	0.50	ND	ND	None	Not detected in immune cells
9	*KRT23*	0.50	Macrophage (3)	Neutrophil (0.9)	None	Not detected in immune cells
10	*MAN2B2*	12	Monocyte (18) Macrophage (17)	ncMonocyte (18) Basophil (16)	**B-cell CD4/CD8 Monocyte Eosinophil Neutrophil**	Low immune cell specificity
11	*MAX*	56.8	**Platelet (2,007)**	**Basophil (670) Eosinophil (542)**	**B-cell CD4/CD8 Eosinophil Neutrophil**	Low immune cell specificity
12	*MRPS25*	5.5	T-cell (60) Monocyte (44)	Memory B-cell (65)	None	Low immune cell specificity
13	*NDUFS2*	29.8	T-cell (73) Monocyte (59)	**Myeloid DC (218) iMonocyte (193)**	Erythrocyte	Low immune cell specificity
14	*PPRC1*	3.7	NK cell (9) T-cell (8)	NK cell (4.1)	None	Low immune cell specificity
15	*RAD23A*	73.1	**T-cell (122) B-cell (120)**	**ncMonocyte (106) iMonocyte (102)**	Erythrocyte	Low immune cell specificity
16	*REPIN1*	17.7	DC (97)	pDC (7.8)	**B-cell Neutrophil**	**Immune cell enhanced (pDC)**
17	*SDR39U1*	9.8	Platelet (48) T-cell (42)	pDC (62) NK cell (60)	None	Low immune specificity
18	*SETBP1*	0.5	DC (47) B-cell (35)	Naïve B-cell (2.9) pDC (2.7)	**Clonal Hematopoeisis**	**Immune cell enhanced (B/pDC)**
19	*SLC14A1*	3.5	T-cell (19) NK cell (11)	T-reg (4.1)	None	**Immune cell enhanced (T-reg)**
20	*SLC18A2*	0.2	Platelet (48) DC (14)	Basophil (60)	None	**Immune cell enriched (basophil)**
21	*SMC4*	2.0	T-cell (87)	Basophil (75)	None	**Immune cell enhanced (basophil)**
22	*SPARC*	33.5	**Platelet (2,130)**	Neutrophil (25) Basophil (10)	**Erythrocyte Neutrophil B lymphopoeisis**	**Group enhanced (neutrophil, basophil, classical monocyte)**
23	*SQLE*	2.0	B-cell (29)	Naïve B-cell (17) Memory B-cell (16.6)	None	Low immune cell specificity
24	*STRIP1/ FAM40A*	10.6	T-cell (18) B-cell (18)	NK cell (16) Memory CD8 (16)	NA	Low immune cell specificity
25	*STX12*	13.7	Macrophage (61) Monocyte (51)	ncMonocyte (41) iMonocyte (40)	**B-cell Monocyte Neutrophil**	Low immune cell specificity
26	*UNC45A*	18.6	Platelet (57)	GdT-cell (11.8) ncMonocyte (11.7) Basophil (11.5)	**B-cell**	Low immune cell specificity
27	*XPC*	13.2	T-cell (61) NK cell (57)	Neutrophil (74)	**CD4/CD8**	Low immune cell specificity

*From GTex (www.gtex.portal.org/home/gene) [5,6] (*n*=755 whole blood samples, median TPM)
‡From the HPA (www.proteinatlas.org/) (*n*=109 blood samples, nTPM) [7]
†From BloodSpot (Haemopedia) DMAP [8,9] – normal human Hematopoeisis: https://servers.binf.ku.dk/bloodspot/?gene=. Gene signatures are derived from DMAP data (www.broadinstitute.org/dmap/home)
**PubMed search (gene name/Hematopoeisis, 9/2023)
Low immune cell specificity = detected in all immune cells at low levels
DC = dendritic cell, GdT = gamma-delta T-cell, iMonocyte = intermediate monocyte, MAIT = mucosal associated invariant T cell, NA = not annotated, ncMonocyte = non-classical monocyte, ND = not detected, pDC = plasmacytoid dendritic cell

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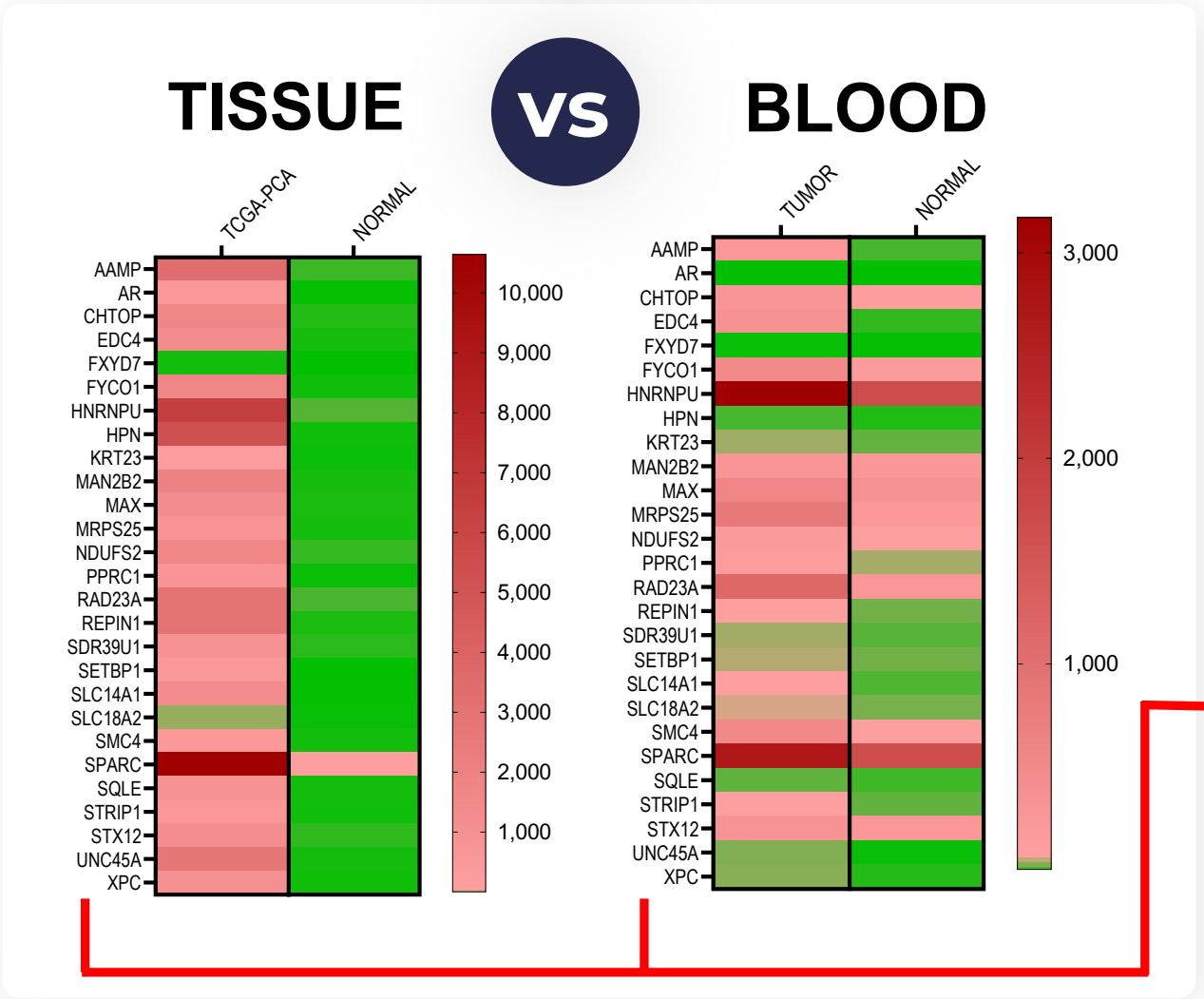
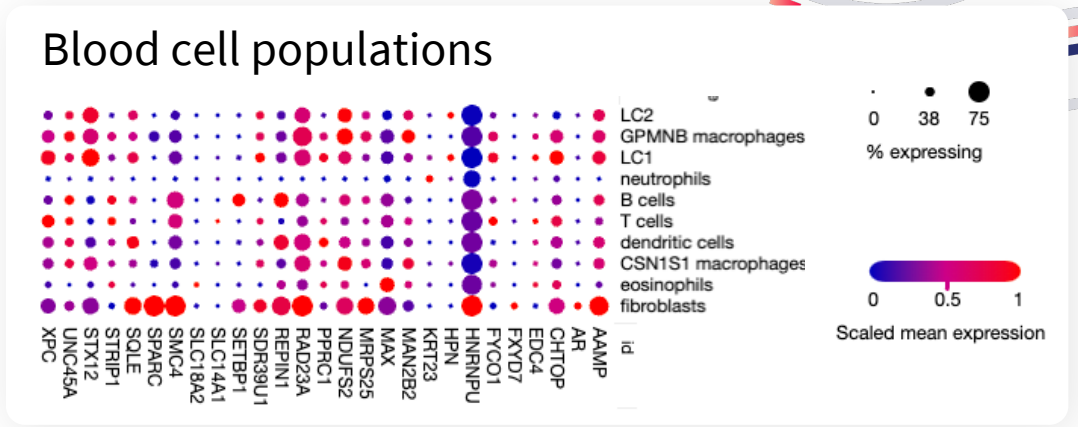
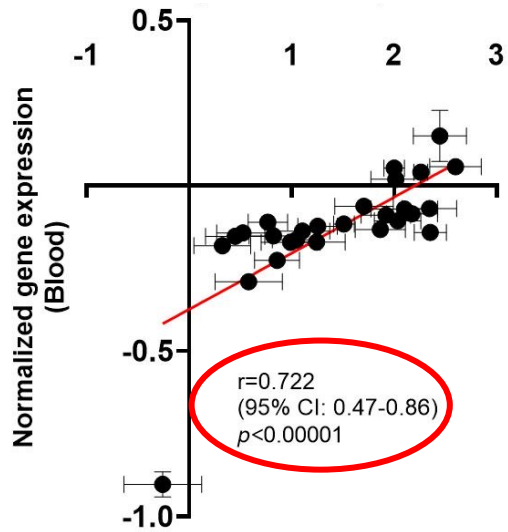
Molecular Recognition

Is it tumor-related or is the message blood-derived?







Tumor
Tissue: Blood Correlation

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Molecular Recognition – Algorithms

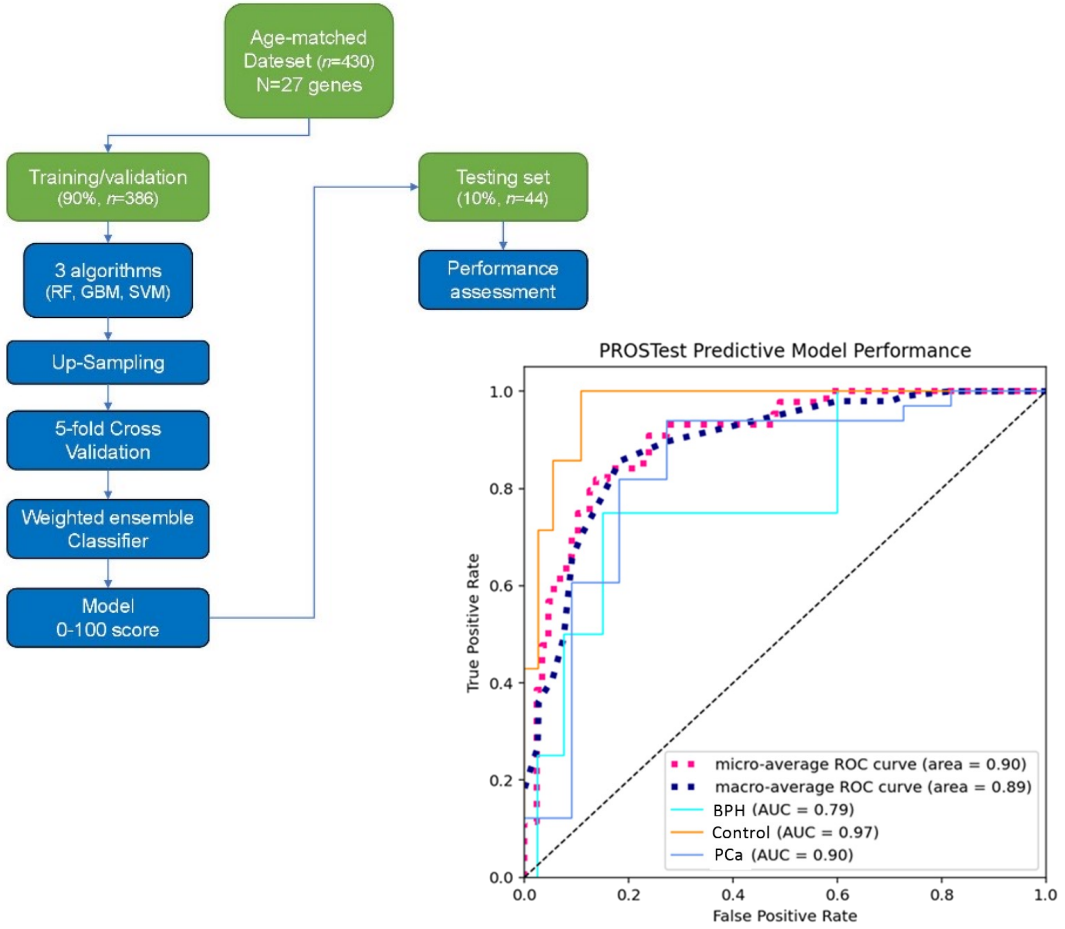
How accurate are blood-based mRNA signatures?

Classifiers function to identify patterns of gene expression and “learn” to assign samples to a specific class (e.g., cancer vs. control).

Hyperparameter optimization (HPO) and feature selection (FS) improve the predictive performance of algorithms

Ensemble-based algorithms consistently outperform other types of classification algorithms

Wren algorithms utilize HPO and FS



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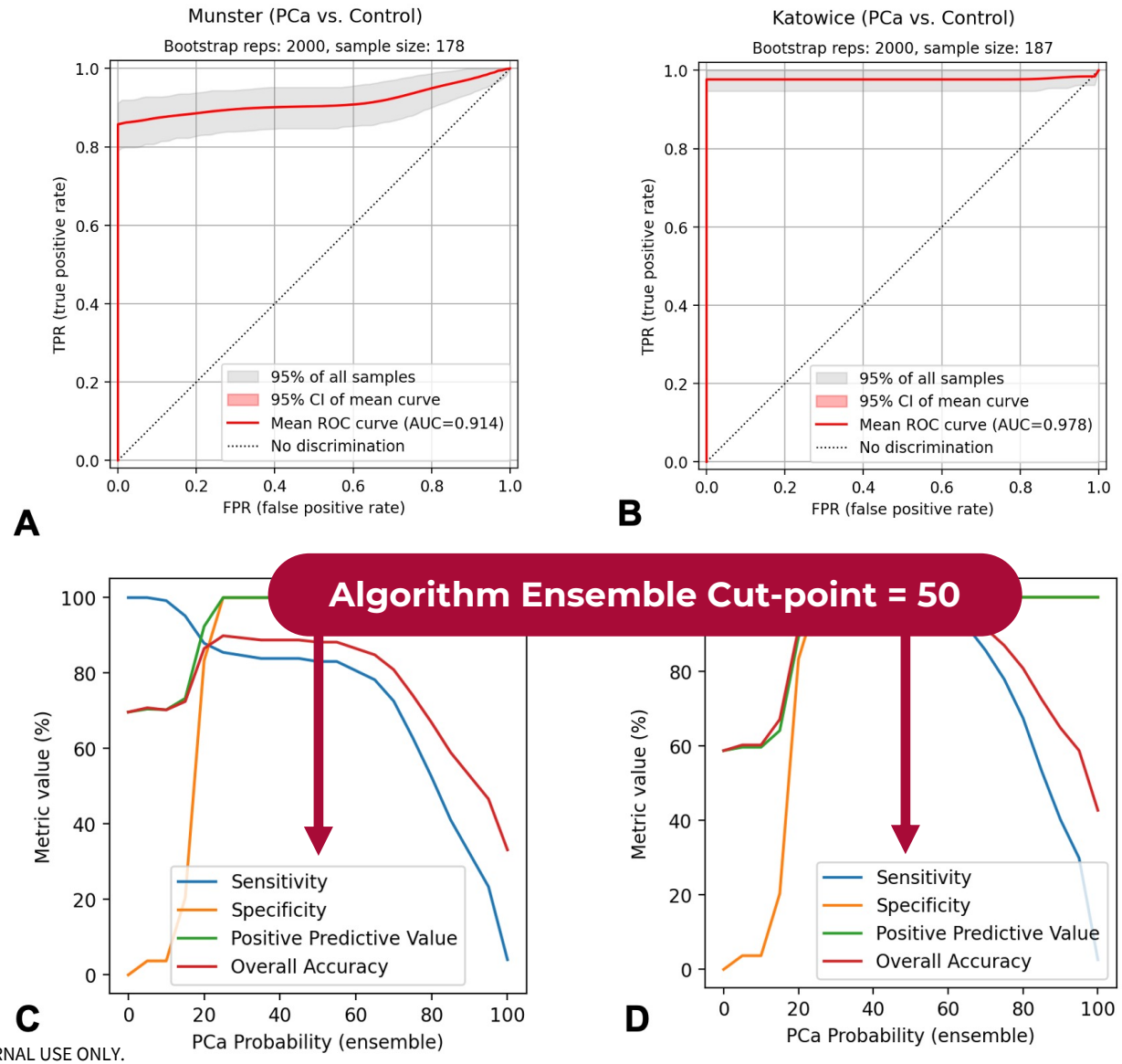
Algorithm Testing



A. Receiver operator curves (ROC) for differentiating age-matched PCa and Controls (Cohort I: *n*=178)

B. (ROC) for differentiating age-matched PCa and Controls (Cohort II: *n*=187)

C. Line plots of PPV, sensitivity, specificity (Cohort I)

D. Line plots of PPV, sensitivity, specificity (Cohort II)

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Algorithm Performance Metrics*

Dataset	Class	AUROC	Sensitivity	Specificity	PPV
Munster (*n*=178)	PCa vs. Control	0.91 (0.913-0.915)	83% (80%-87%)	100% (96%-100%)	100% (95%-100%s)
Katowice (*n*=187)	PCa vs. Control	0.98 (0.977-0.979	94% (92%-96%)	100% (96%-100%)	100% (96%-100%)

95% Confidence Intervals are shown in parentheses. PPV=Positive Predictive Model.

*Using the Algorithm Ensemble Cut-point = 50 (scale 0-100)

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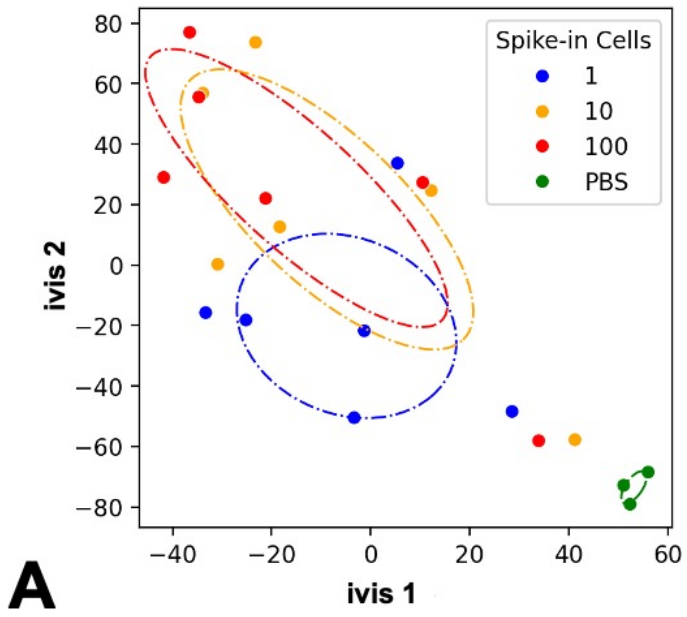
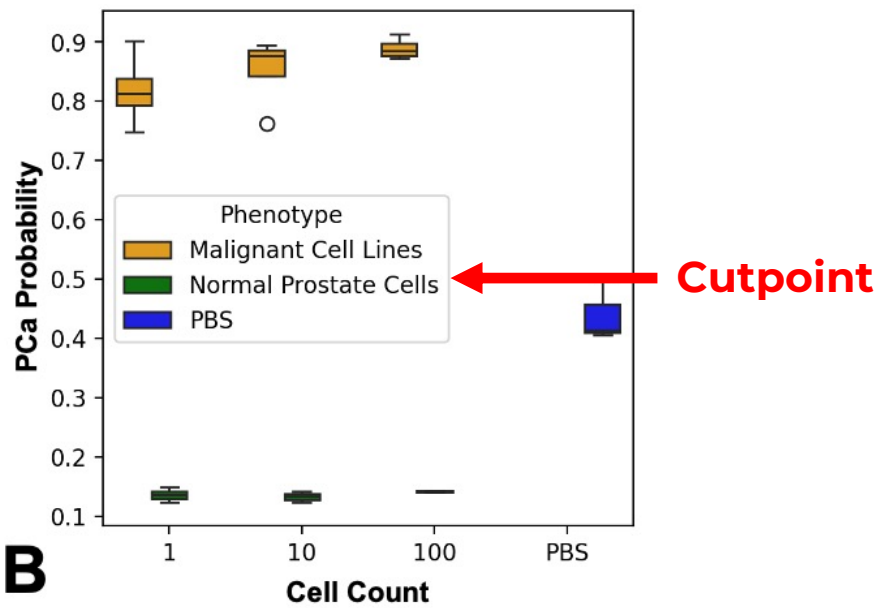
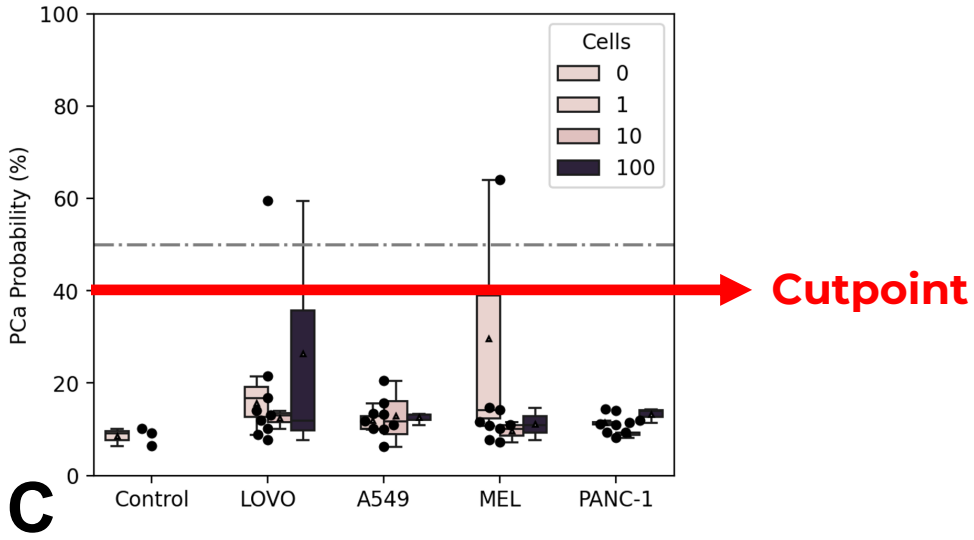
Blood Spike-in studies







A. Scatterplot showing two-dimensional twin neural network (Ivis) embedding of the model feature values in spike-in experiments.

B. Boxplots of spike-in blood algorithm scores – prostate cancer cell lines (*n*=6)

C. Boxplots of spike-in blood scores – non-prostate cancer cell lines (*n*=4)

Normal prostate:
PWRE-1, RWPE-1

Malignant PCa:
DU145, LnVAP, MDA PCa2b, PC-3

LOVO = colon
A549 = lung
MEL = A375/melanoma
PANC-1 = pancreas

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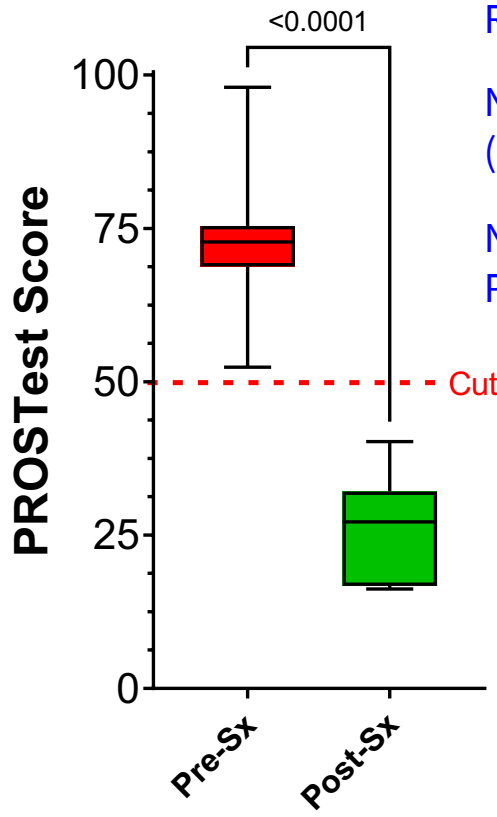
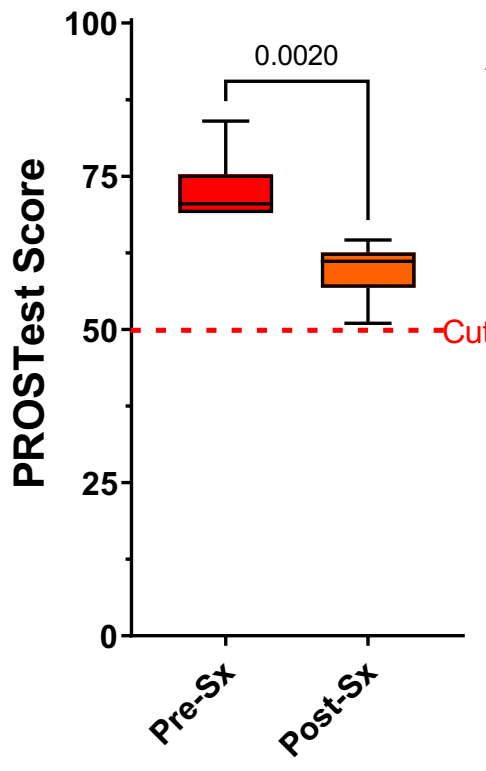
Surgery and Blood Gene expression
(Radical Prostatectomy cohort)



R0: *n*=37

Normal PSA (<0.1ng/mL)

Negative ^{68}Ga-PSMA image



R1: *n*=10

Abnormal PO PSA (>0.1ng/mL)

Positive ^{68}Ga-PSMA image

Complete tumor removal removes source of the "PROSTest" signal

Blood gene expression "PROSTest" is derived from tumor tissue

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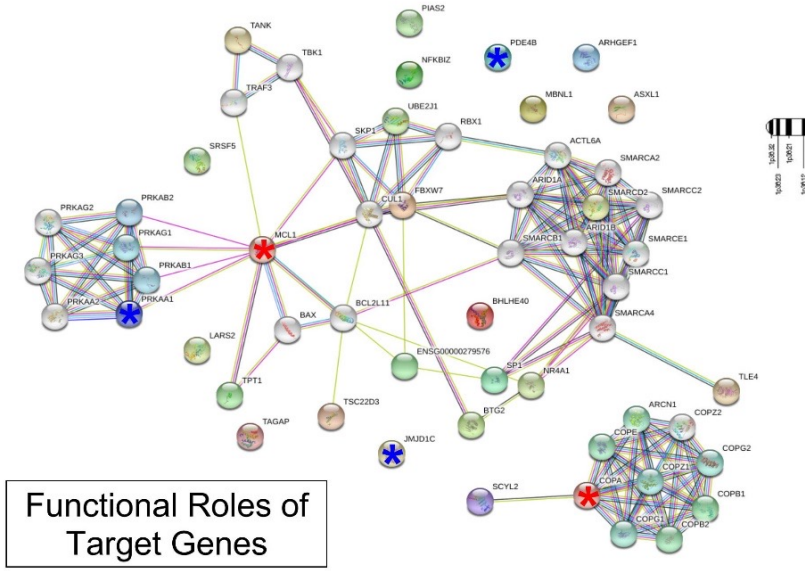
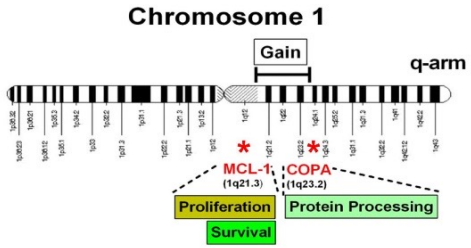
Multiple Myeloma



Functional Roles of Target Genes

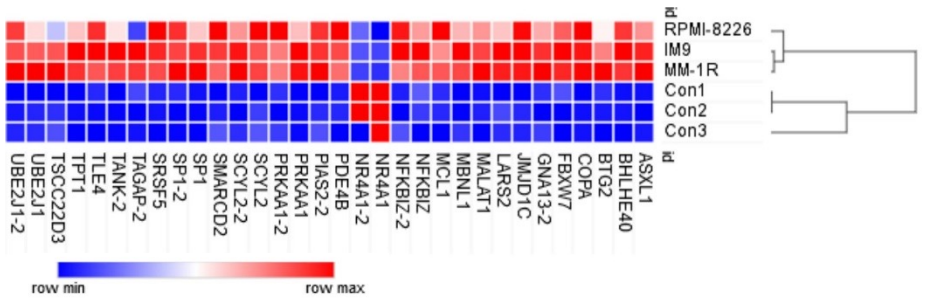
Apoptosis	Immune Response	Phenotype	Protein Processing	Proliferation	RNA Processing	Survival
BTG2 NFKBIZ	LARS2 NFKBIZ NR4A1 TAGAP TANK TLE4 TSC22D3	NR4A1 SCYL2 SMARCD2 TLE4	COPA1 LARS2 SCYL2 UBE2J1	GNA13 JMJD1C MALAT1 MCL-1 PDE4B	MBNL1 SRSF5	MCL-1 NFKBIZ PDE4B PRKAA1 TSC22D3 UBE2J1



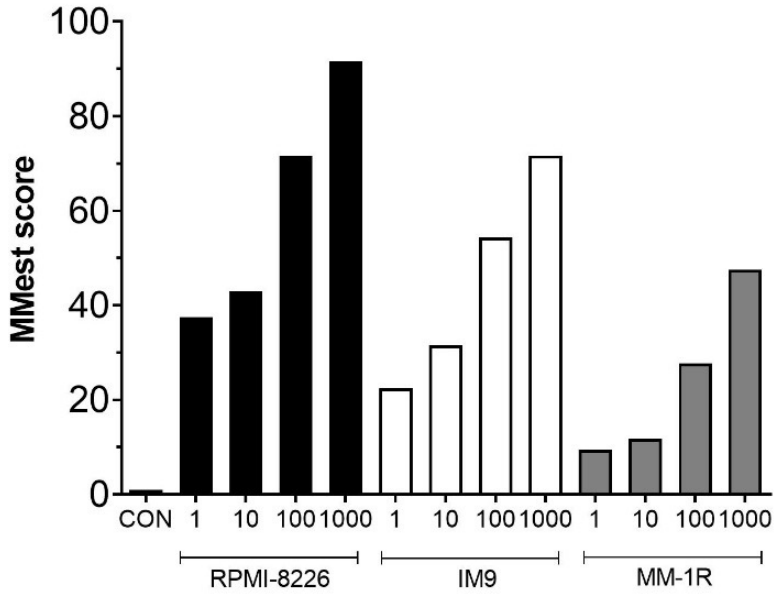
*** Potential Drug Targets**
PRKAA1 (AMP)
PDE4B (AKT/mTOR)
JMJD1C (anti-leukemics)

MALAT
Oncogene
(long non-coding RNA)

Hierarchical clustering

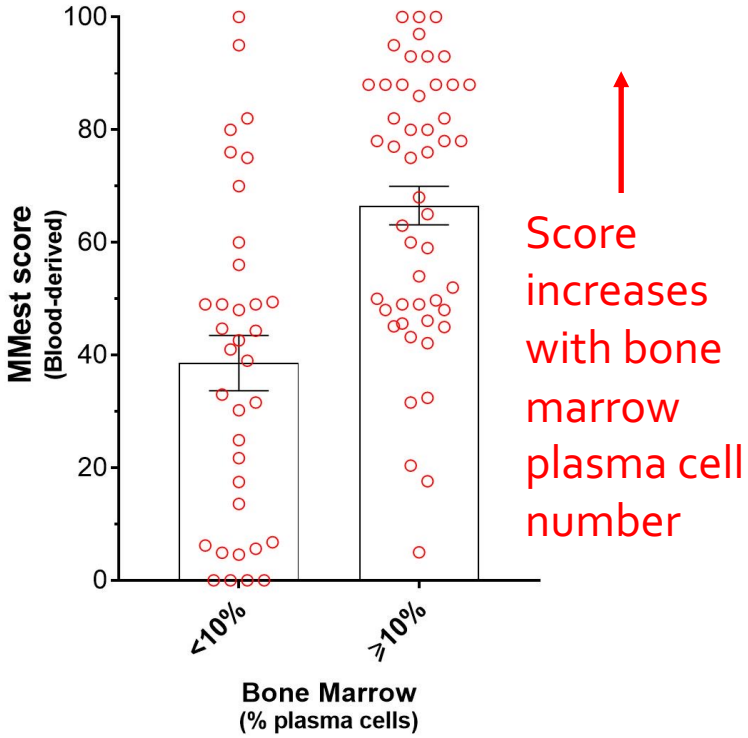


Blood spike-in study



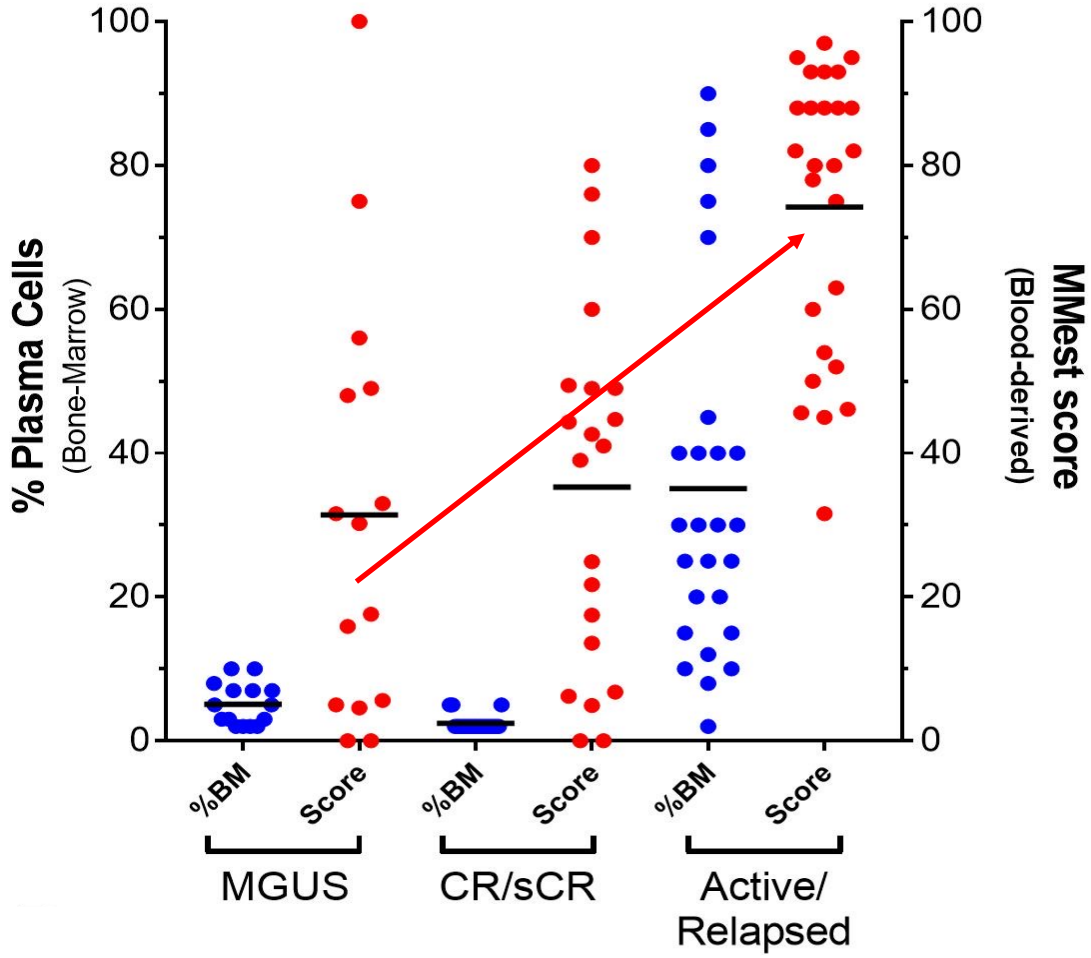
Multiple Myeloma

25-gene blood algorithm score (MMest)



Score increases with bone marrow plasma cell number

Pearson correlation: r=0.29, $p<0.006$, $n=84$)



Horizontal black lines = mean levels
CR = complete remission

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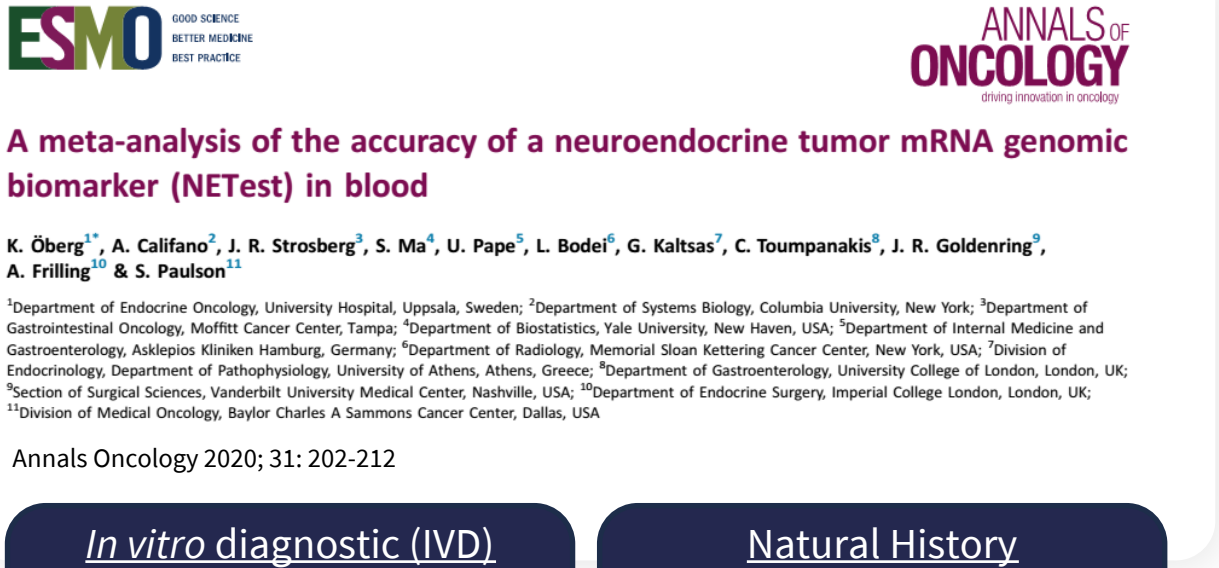
Neuroendocrine Tumor – NETest®



ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

A meta-analysis of the accuracy of a neuroendocrine tumor mRNA genomic biomarker (NETest) in blood

K. Öberg[1*], A. Califano[2], J. R. Strosberg[3], S. Ma[4], U. Pape[5], L. Bodei[6], G. Kaltsas[7], C. Toumpanakis[8], J. R. Goldenring[9], A. Frilling[10] & S. Paulson[11]

[1]Department of Endocrine Oncology, University Hospital, Uppsala, Sweden; [2]Department of Systems Biology, Columbia University, New York; [3]Department of Gastrointestinal Oncology, Moffitt Cancer Center, Tampa; [4]Department of Biostatistics, Yale University, New Haven, USA; [5]Department of Internal Medicine and Gastroenterology, Asklepios Kliniken Hamburg, Germany; [6]Department of Radiology, Memorial Sloan Kettering Cancer Center, New York, USA; [7]Division of Endocrinology, Department of Pathophysiology, University of Athens, Athens, Greece; [8]Department of Gastroenterology, University College of London, London, UK; [9]Section of Surgical Sciences, Vanderbilt University Medical Center, Nashville, USA; [10]Department of Endocrine Surgery, Imperial College London, London, UK; [11]Division of Medical Oncology, Baylor Charles A Sammons Cancer Center, Dallas, USA

Annals Oncology 2020; 31: 202-212

In vitro diagnostic (IVD)	Natural History
Accuracy: 96%	**Accuracy: 94%**
Sensitivity: 94.4%	Sensitivity: 99.6%
Specificity: 98.7%	Specificity: 99.4%

Disease Status	Monitor Therapy
Accuracy: 86%	**Accuracy: 97%**
Sensitivity: 83.1%	Sensitivity: 90.1%
Specificity: 89.4%	Specificity: 99.7%

The NETest is an accurate biomarker suitable for clinical use in NET disease management.

The meta-analysis supports the utility of the NETest as an IVD to establish a diagnosis and monitor therapeutic efficacy.

The use of this as a biomarker provides information relevant to NET management consistent with observations regarding utility of liquid biopsies in other oncological disciplines.

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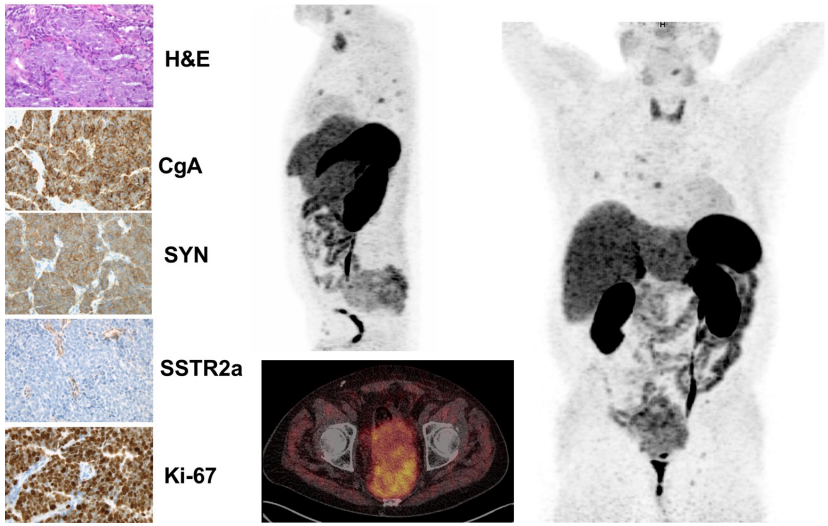
Blood-based detection of Neuroendocrine Differentiation

NETest®

Tumor Neuroendocrine-like Differentiation(Neld/Ned)

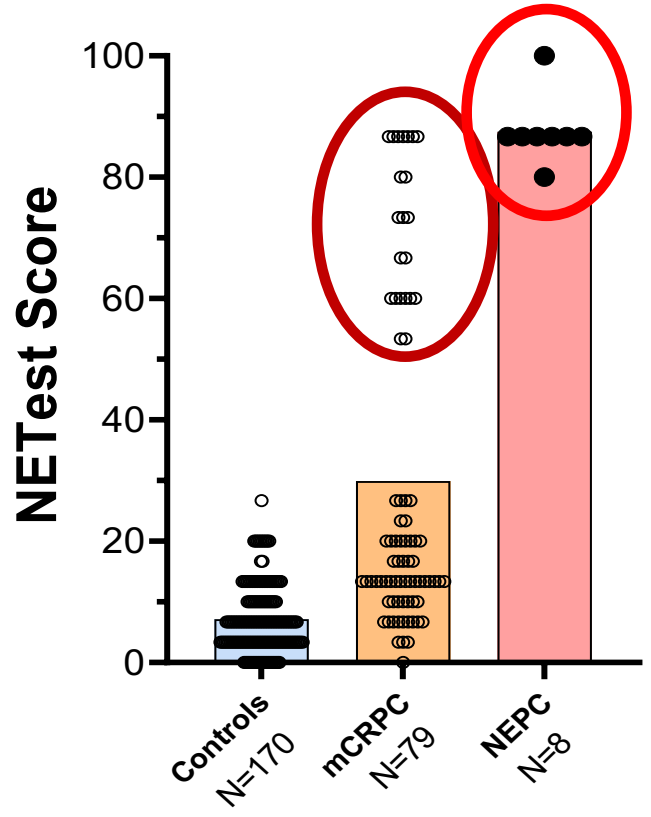


Prostate (PRAD)

Lung (LUAD)

Colon (COAD)

Early detection
Therapy Failure
(e.g., ADT, targeted therapies)



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NETest – A Commercial Success

Over 9,000 NETests used in numerous global studies with leading US and international academic and clinical institutions.

Successful and profitable NETest™ Pharma collaborations

xencor

Phase 1 Clinical trial of XmAb®18087:
NETest biomarker for treatment efficacy
- XmAb18087 engages the immune system against tumors by binding to somatostatin receptor 2 (SSTR2) and CD3.

NIH NATIONAL CANCER INSTITUTE

Von Hippel Lindau germline tumors:
NETest: Diagnostic biomarker

NETest: Diagnostic biomarker:
Paragangliomas and Pheochromocytomas

康圣环球 Kindstar Global

NETest: Clinical testing
Diagnosis, monitoring, surgery, PRRT
Beijing, China, Peking Medical University
Precision Medicine Oncology

RadioMedix INNOVATING THERANOSTICS

Phase 2 Open label study of 212Pb-AlphaMedix targeted alpha therapy:
NETest biomarker for treatment efficacy
- Somatostatin receptor 2 (SSTR2) radiotherapy targeting metastatic NETs.

labcorp

NETest: Clinical testing
PRRT prediction, monitoring
Precision Medicine Oncology USA

KlinicSync

NETest: Clinical testing
Diagnosis, monitoring, PRRT
Mexico, Precision Medicine Oncology

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Our Approach: Assay Development

mRNA based disease biomarkers and patient clinical data are the basis of our diagnostic approach

Discover mRNA-based Biomarkers

Identify genes with RNA expression levels significantly different from controls or between disease states

Incorporate Patient Data

Utilizing ML algorithms to create hyperparametric gene expression data from patient demographics allows us to go beyond simple diagnostics

Develop Diagnostic Approach

Diagnostic, prognostic, and monitoring outputs provide insight on patient journey using either blood or saliva samples

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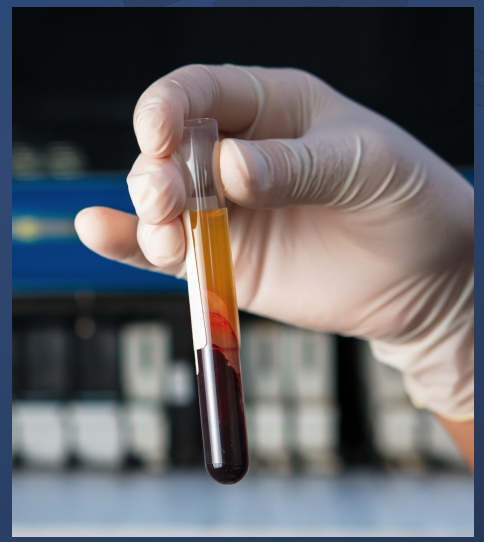
Appendix



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Wren Laboratories: Founded 2012

Platform

A molecular diagnostics company that develops mRNA-based biomarkers for assessment with a suite of AI-enabled multianalyte algorithms to identify and characterize a range of cancers and other diseases

Proven Success

Innovator of molecular signatures for cancer diagnosis and management. Our liquid biopsy-based diagnostics use molecular science to uncover precise information about cancer in real-time, enhancing pathology and imaging.

Available Diagnostics

NETest (2014)

PPQ (2022)

SARS-CoV-2 (2021)

Coming soon :

PROSTest 2024

Credentials

CLIA Certified

CAP Accredited

CT Clinical Lab License CL-0996

New York Dept of Health

Clinical Lab Permit PFI: 9138

Florida License 800027786, certificate 101250

PA Laboratory ID: 34347

California Lab ID: COS00800634

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The Team

The Wren Laboratories team is comprised of individuals with expertise ranging from medical, clinical, research and commercial diagnostic execution.

Irvin M. Modlin
Founder, Clinical & Scientific Consultant
MD, Ph.D., DSc

Daniel Buck
Managing Director
MBA, MPH

Mark Kidd
Scientific & Laboratory Director
Ph.D., DABCC

Ignat Drozdov
Scientific & Clinical AI Consultant
MD, Ph.D.

Andi Neugarten
Corporate & Business Development
B, Acc, CA.SA

Mark Harman
Medical & Clinical Affairs
MD, MBA, MS ,BCMAS

Srinivas Koduru
Transcriptomics
PhD

Tracy Auster
Laboratory Manager
ASCP, AGT

EJ Vongher
Marketing Director

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Wren Laboratories

Molecular-based tools that accurately capture tumor pathobiology

Diagnosis

Treatment Prediction

Monitoring

Disease Prognosis

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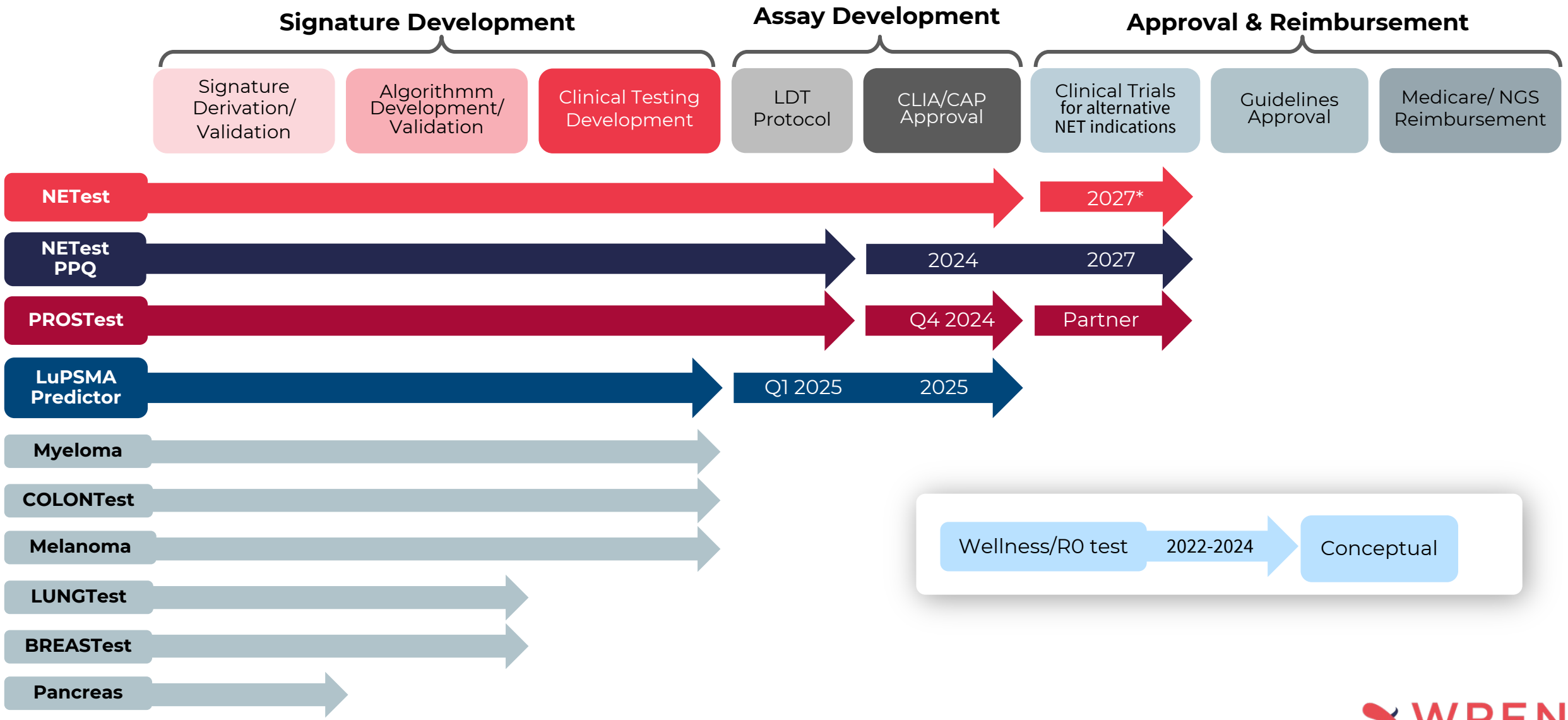
WREN Test Pipeline: A Development Timeline



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