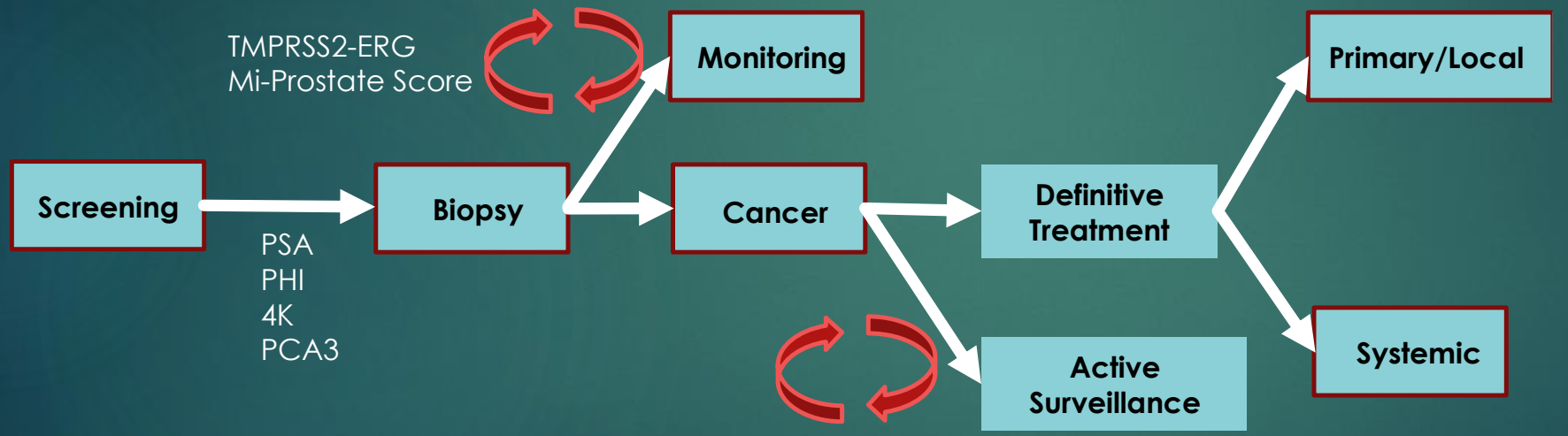
Prostate Collaborative Group

John Semmes and Martin Sanda

PCPT Ian Thompson, (ERSPC, PLCO, etc)

Avoiding Overtreatment



RISK GROUPS

Identification of aggressive disease

Prostate Cancer Upgrading Study

Robin Leach

PURPOSE: A multi-institutional study to identify GS 7 or greater cancer in men diagnosed GS≤ 6.

- PIs: Ian Thompson , Robin Leach, Martin Sanda, Paul Boutros
- Data Coordination: Fred Hutchinson Cancer Res Ctr
- Pathology: Dean Troyer, EVMS
- Biostatistics: Yingye Zheng, Fred Hutchinson Cancer Res Ctr

Pending Round 1	Ineligible Round 1	Confirmed Round 1	Biopsy Sent to Review	Ineligible Round 2	Confirmed Round 2 With Post DRE Urine	Confirmed Round 2 without Post-DRE Urine
6	55	354*	223+	52	197#	70

*Final goal 240 with 200 "complete sets" to be used for sequencing phase

*A distribution plan is in place and committee established.

EDRN PROSTATE MRI BIOMARKER STUDY

John Wei

Integration of MRI into the initial biopsy setting
Performance with validated laboratory biomarkers

Prospective Longitudinal Study
Target enrollment: 1500

UPDATE:
9 Sites Online
78 Cases Enrolled
COVID

MRI Active Surveillance

Michael Liss

Associate Membership
And
BDL Collaborative Restricted Funds
Supported Study

Harvard, Emory, Wash U CVC

Martin Sanda

Development of New Biomarkers

(Aim) Biomarker	1. Readiness	2. Intended Use	3. Type of biomarker	4. Specimen	5. Parameters
1) Phi-PCA3 combination	in clinical use (expanded indication)	Screening, surveillance (reduce un-necessary bx)	Protein (phi), RNA (PCA3)	Serum *(phi)*, post-DRE urine (PCA3)	Increase specificity at high sensitivity
2) Urine EV Transcriptome	CLIA, clinical grade platform	Screening, surveillance (reduce un-necessary bx)	RNA	post-DRE urine	Increase sensitivity, specificity
3) Flucyclovine (Axumin) PET	in clinical use (expanded indication)	Detect occult metastases	Metabolic Radiotracer	PET imaging	Increase sensitivity over conventional imaging

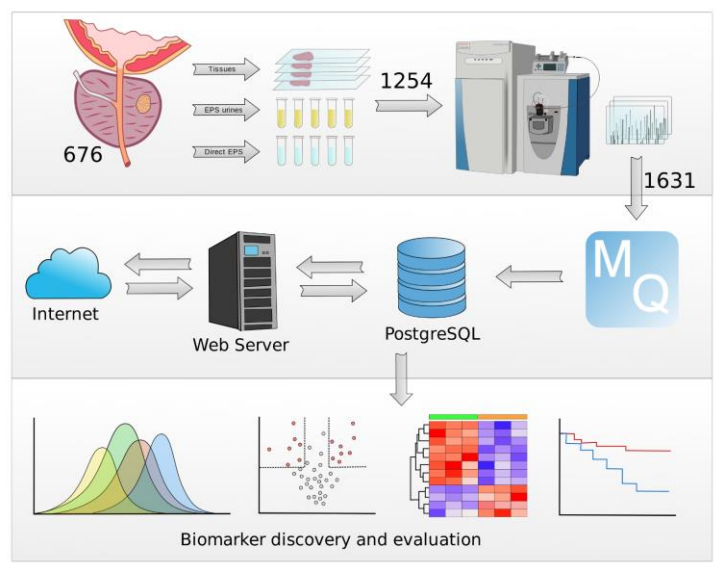
EDRN Team Projects

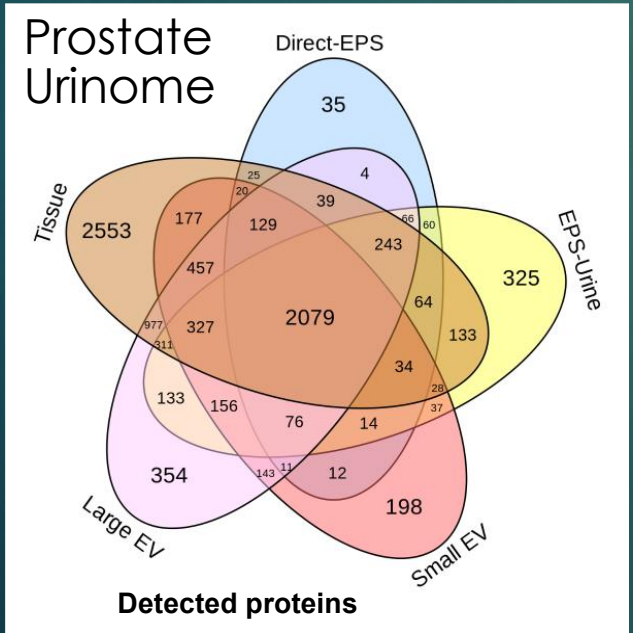
Multi-site Trial	EDRN Sites	Endpoint	Biomarkers
Upgrading Study *Thompson, Leach, Sanda, et al*	DMCC; CVC (Emory, UTHSC-SA); Multisite Trial Group; BDL's (CPDR, EVMS, Hopkins Michigan); BRL's (Hopkins, PNNL)	Outperform biopsy in discerning aggressive vs indolent cancer (Upgrading at Prostatectomy)	Serum: *phi,* Tissue: RNA, RNA-Seq Urine: PCA3, T2:Erg, Targeted RNA-Seq, Transcriptome, Proteoglycomics
Combining MRI+ Serum and Urine Biomarkers *Wei et al*	DMCC; New Multi-center Imaging Group, BDL's, BRL, CVC's	Aggressive Prostate cancer at initial biopsy	Serum: *phi,* Urine: PCA3, T2:Erg, Transcriptome, Targeted RNA-Seq, Proteoglycomics

*The CVC provided 7,955 samples from from 1,923 patients

EVMS, U Toronto, UCLA BDL

Paul Boutros, Thomas Kislinger, Julius Nyalwidhe, John Semmes





Web Portal

Clinical Data
Protein Spectral Data

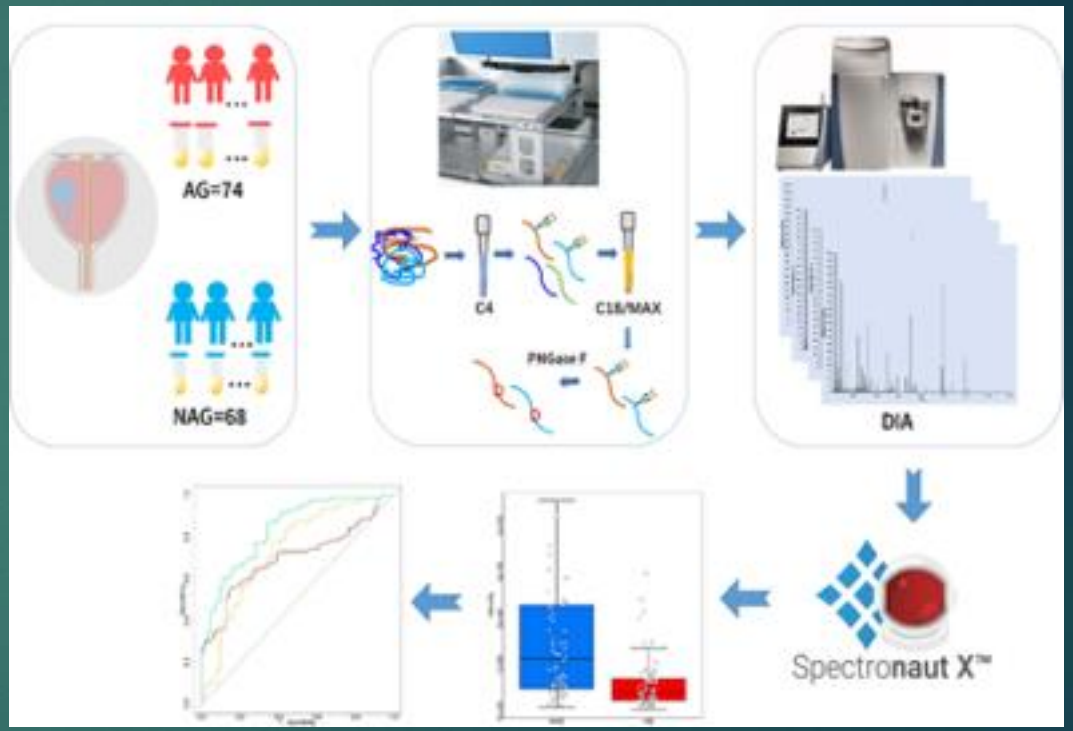
*EARLY DETECTION OF AGGRESSIVE DISEASE

*UPGRADING STUDY

*RISK STRATIFICATION

Johns Hopkins University School of Medicine BDL

Established high throughput glycoproteomic biomarker development workflow



Fucosylated Serrum PSA
Urinary ACPP
Urinary CD63
Urinary LOX
Urinary CLU
Urinary PSA

Pre-validation

A Tissue-Based 5-protein Classifier for Prediction of Prostate Cancer Progression

Tao Lui

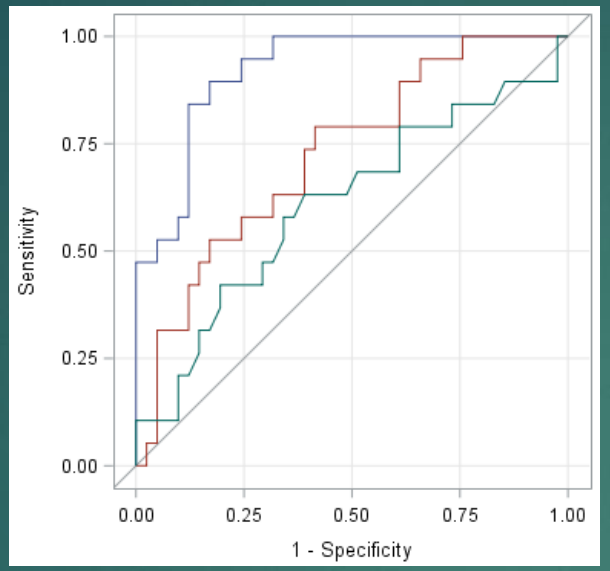
PNNL

PCa prognosis associated genes	Other PCa associated genes	Other cancer related genes
AKT1	AMACR	BRAF
ANXA2	CRISP3	CAMKK2
AR	pan-ERG	EGFR
AURKA	ERG8	HIF1A
CCND1	ETV1	HPN (TMPRSS1)
CDKN1A	FOLH1 (PSMA)	HSPB1
EZH2	HOXC6	MMP2
FGFR1	KLK2	MMP9
MUC1	KLK3 (PSA)	PDGFRB
MUC6	KLK11	PIK3CA
MYC	MYO6	PLA2G7
MYCN	NPY	ODC1
NCOA2	PSGR	RAF1
PMP22	SPARC	SERPINI1
SMAD4	TWIST1	STAT3
SPINK1		TGFB1
SPP1 (OPN)		TP53
TFF3		TPM2
		VEGFA

52 gene targets

(*Oncotarget 2019, 10, 6466–83*)

Developed PRISM-SRM-MS assays



Risk stratification
Predicting aggressive disease post RP

Radical prostatectomy 338 FFPE (CPDR) blinded
distant metastasis (n=53): ≥ 1 year post-RP
biochemical recurrence (n=124): ≥ 1 year post-RP
no progression (n=161): after ≥ 10 years post-RP

TGFB1, SPARC, FOLH1, PSA, CAMKK2

	AUC	95% CI		p-value
Biopsy SOC alone	0.73	0.59	0.86	Ref
Biopsy SOC + protein classifier	0.92	0.86	0.99	0.001
Diagnosis PSA alone	0.61	0.44	0.77	0.226

Transfer to serum
Independent testing

Gyorgy Petrovics

CPDR

Development of race informed marker panel and **urine exosomal RNA-based** assay for the **early detection of aggressive prostate cancer**

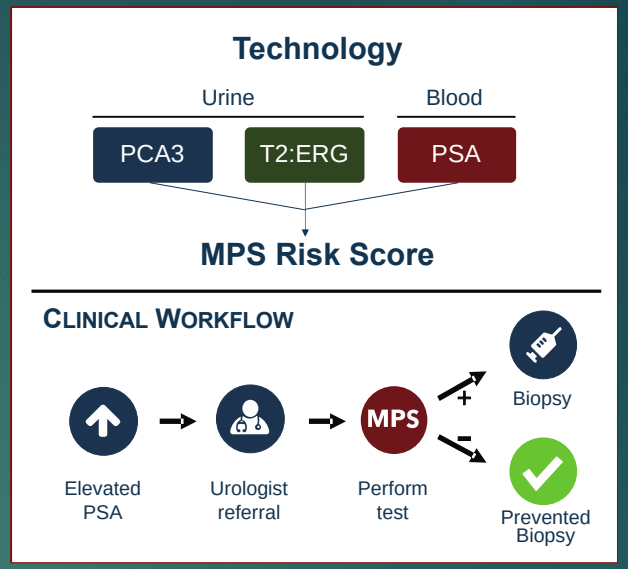
Stratification by **ERG in a large racially diverse (AA, CA) DOD prostate cancer cohort**

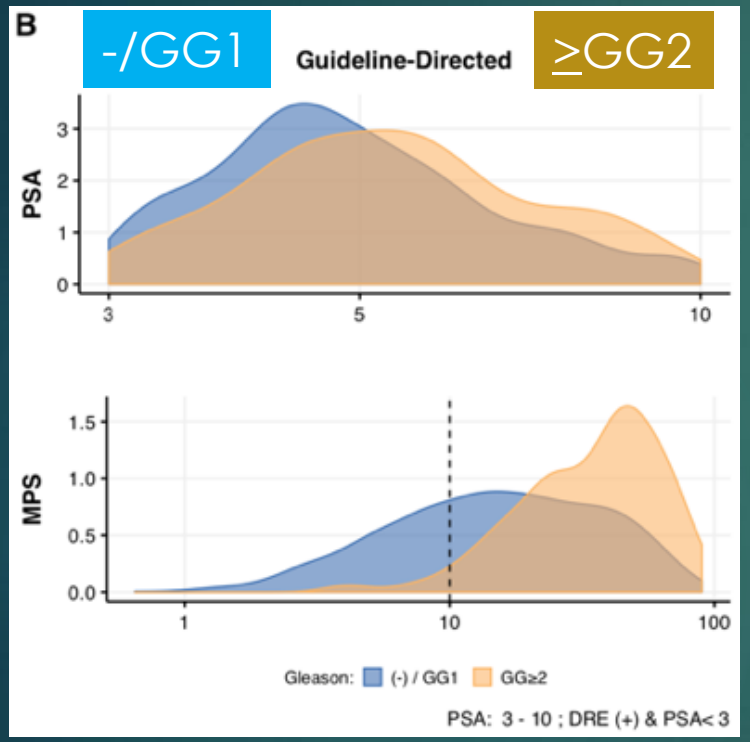
Molecular profiling of radical prostatectomy tissue from patients with no sign of progression identifies ERG as the strongest independent **predictor of recurrence** using **NanoString technology**

5 Current EDRN Collaborations
EDRN-China Initiative

University of Michigan BDL

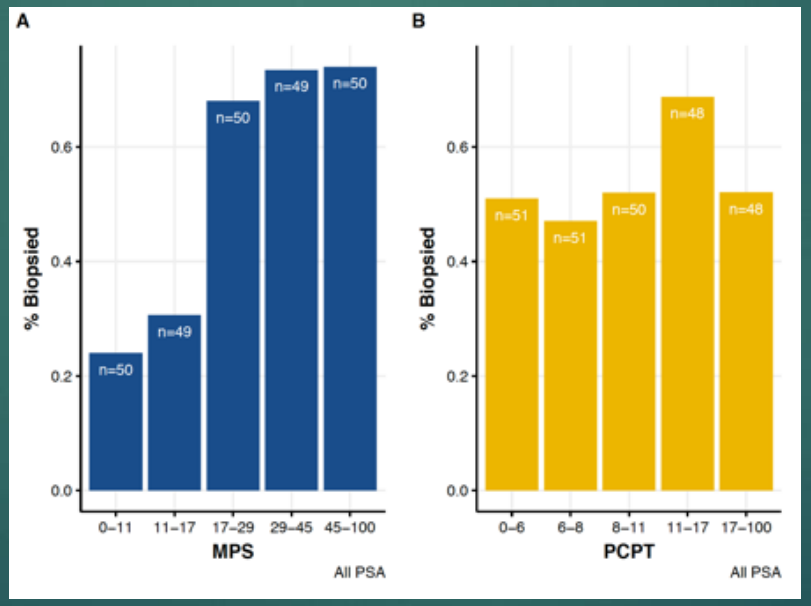
Arul Chinnaiyan



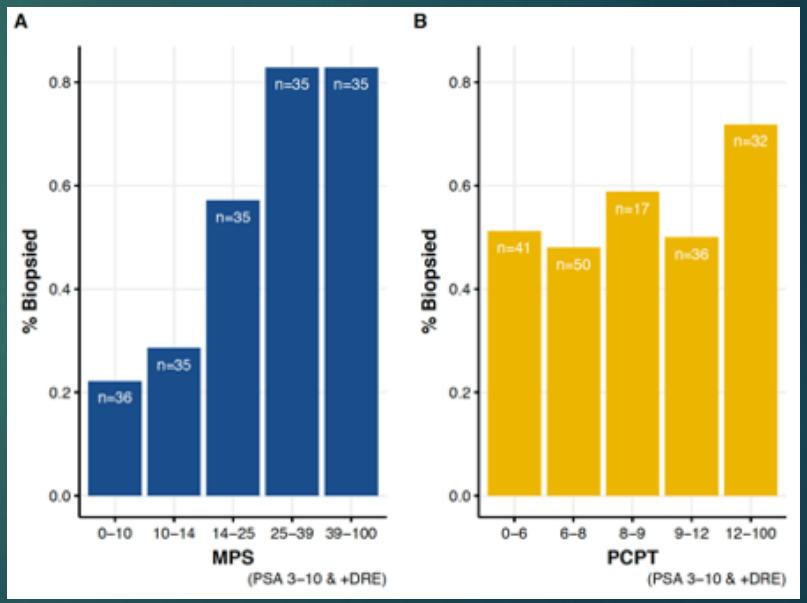


*Clinical performance.

PSA



PSA 3-10 & =DRE

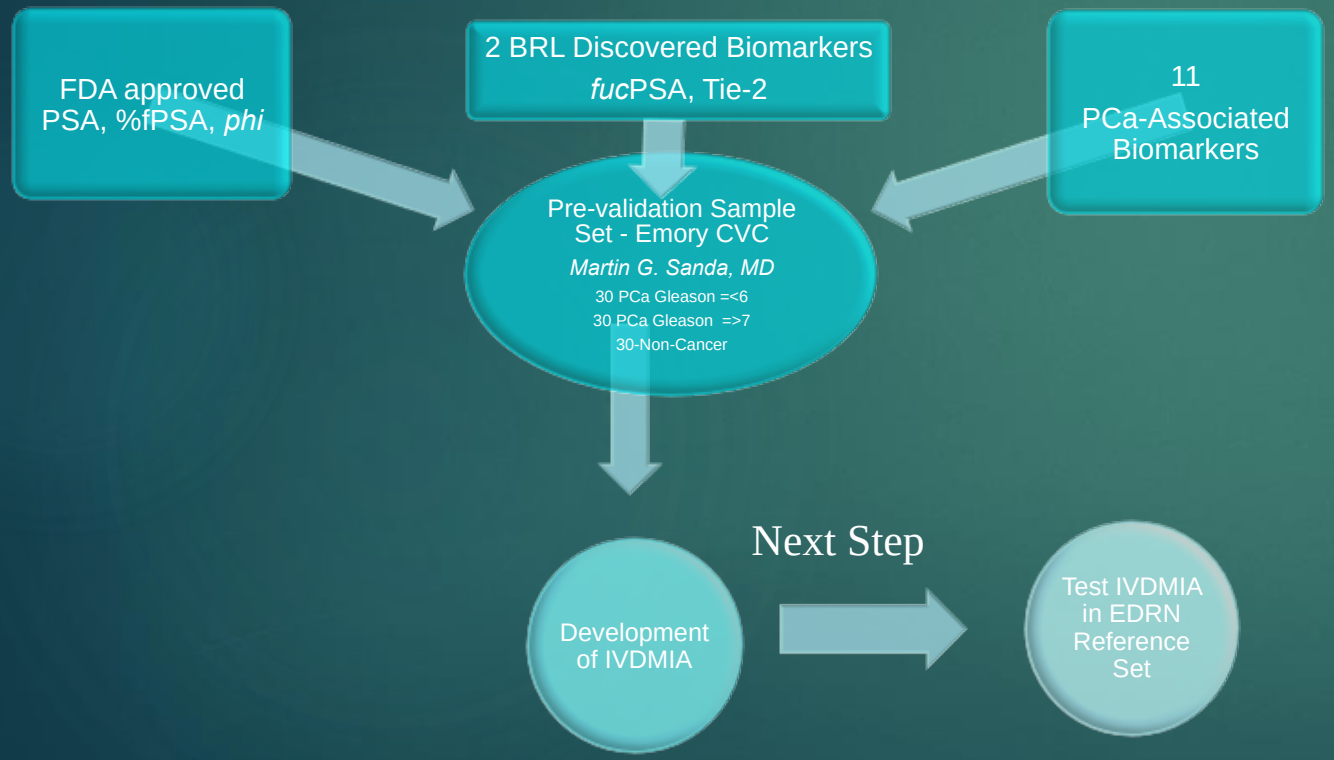


*Evaluation of Clinical Utility

Johns Hopkins University School of Medicine, BVL

Dan Chan

Development of an IVDMIA for Aggressive Prostate Cancer



MiCheck test a current IVDMIA for aggressive prostate cancer Collaboration with Minomic Ltd

- MiCheck is an IVDMIA for aggressive prostate cancer: PSA, patient age, DRE, Leptin, IL-7, VEGF, Glypican-1.
- Developed by Minomic Ltd.
- Agreement with Cirrus Dx, a **CLIA lab.**
- MiCheck performed as an **LDT** (lab developed test).

EDRN Ideally Suited to Leverage Collaboration with Industry to Optimize Biomarker Panels for Clinical Utility and Acceptance

Prostate Collaborative Group SWOT

Strengths

- **Highly Innovative Discovery that Integrates novel technologies into biomarker development workflows**
- **Network focused on design and execution of fit-to-purpose biomarker development.**
- **Existing collaborations with commercial partners.**
- **EDRN Structure Provides Resources for Biomarker Discovery, Validation Design & Implementation.**
- **Network Supported Multi-institutional involvement in the full spectrum of biomarker development.**
- Early integration of Clinical Imaging
- Significant experience in biomarker validation.
- Large clinical cohorts and specimen reference sets designed to accelerate biomarker validation.
- New markers brought to commercialization approval and clinical use.
- Unbiased third part analyses biomarker performance.

Weaknesses

- **EDRN thus far excluded from conducting screening trials.**
- **Lack of formal integration with other parts of the cancer disease continuum.**
- **Lack of support for health economics and implementation sciences.**
- **Lack of a career development for new investigators.**
- Limited clinical scope due to program restrictions.
- Limited interaction between collaborative groups.
- Lack of Kidney and Bladder Cancer programs.
- Low Representation of radiology and medical oncology.
- Cumbersome data access and sharing.

Prostate Collaborative Group SWOT

- **Partnering with NCI/NIH networks for detection applications, biomarker discovery/repurposing, and providing data analysis.**
- **Enhance partnerships with FDA and commercial teams to streamline implementation and approval.**
- **Consider ancestral diversity in all stages of biomarker development.**
- **Emerging technologies in single cell analysis to probe tumor heterogeneity.**
- **Multimodality biomarkers including imaging and Integration of digital pathology.**
- Pan-cancer detection strategies – enhanced interactions between collaborative groups (eg BRCA2).
- Optimize awareness and utilization of samples from network cohorts beyond EDRN.
- Accessing multi-center sample sets for discovery and validation.

Opportunities

- **Commercial development of biomarkers not having clinical validity.**
- **Changes in SOC for screening, detection, diagnosis can impinge utility of biomarker development.**
- **Risk that research is perceived as clinically incremental.**
- **Rapid evolution of biomarker science.**
- Impact of COVID on cancer life history.
- Challenges for new investigators with fresh ideas to get funding.
- Reduction in funding.

Threats

New Screening Trials

- **New screening trials using established biomarkers as foundation: discovery to validation on collected specimens to enhance screening effectiveness.**

Screening trials in prostate cancer would benefit patients and EDRN research objectives

EDRN is uniquely positioned to lead screening trials

Screening trials require a significant investment of time, energy and money

Set initial goals with achievable objectives:
targeted surrogate outcomes
Discovery to pre-validation

OUR SPACE

Smart Biomarker Discovery
Collaborative Team Science
Infrastructure to Move Discovery toward the Clinic

Future Directions:

- Clinical Utility Studies
- Health Economics
- Industrial Partnerships
- Early Investigator Training

5 minute Q&A

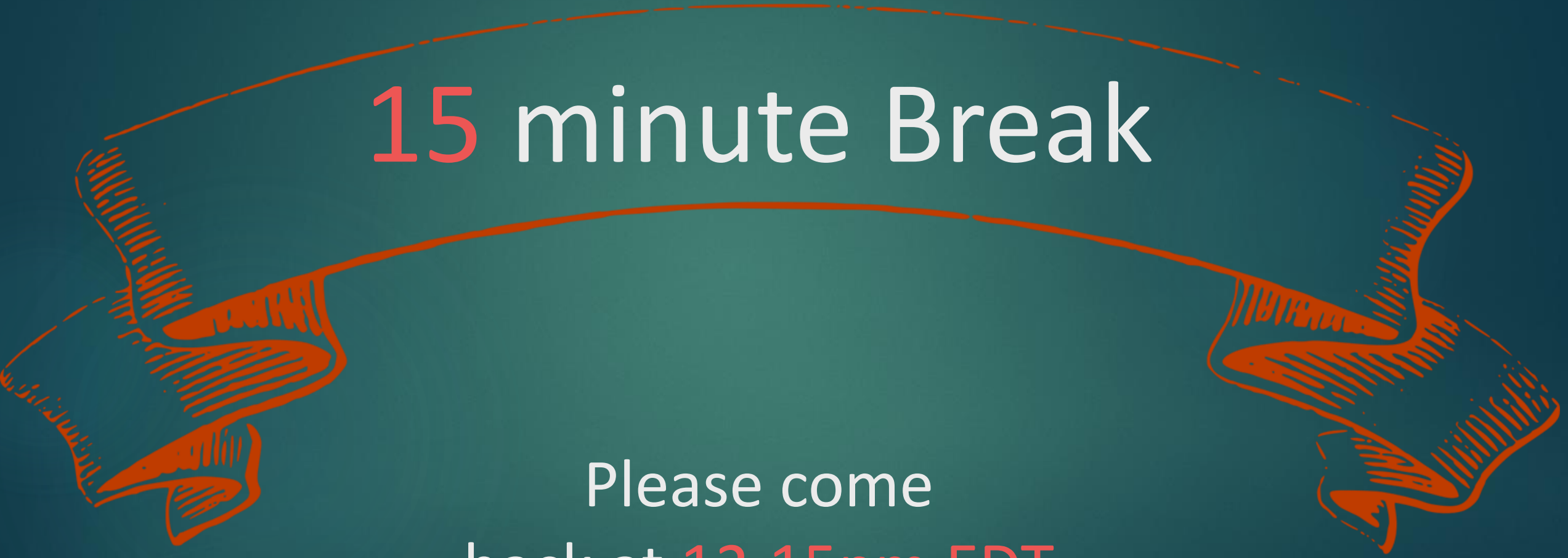
SC Chair/Co-Chair

feed Zoom Q&A to presenter and Track Time

NCI and Production Team

flag Q&A, answer Chat and Slack

15 minute Break



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Enhancement of Team Structure

- **Find ways to expand teams through Partnerships with other NCI/NIH networks for detection applications, biomarker discovery/repurposing, and providing data analysis.**
- Enhance interactions between collaborative groups, especially in pursuit of Pan-cancer detection strategies.
- **Enhance partnerships with FDA and commercial teams to streamline implementation and approval.**
- **Enhance Teams to integrate all elements of the cancer disease continuum.**
  - **Healthcare economics**
  - **Test implementation**
  - **Patient benefit**
- Have a means to train future researchers in productive team science
- Optimize awareness and utilization of samples from network cohorts beyond EDRN.