

**Early  
Detection  
Research  
Network**



# Reissuance Request

**Peter Greenwald, MD, DrPH**

**Sudhir Srivastava, PhD, MPH**

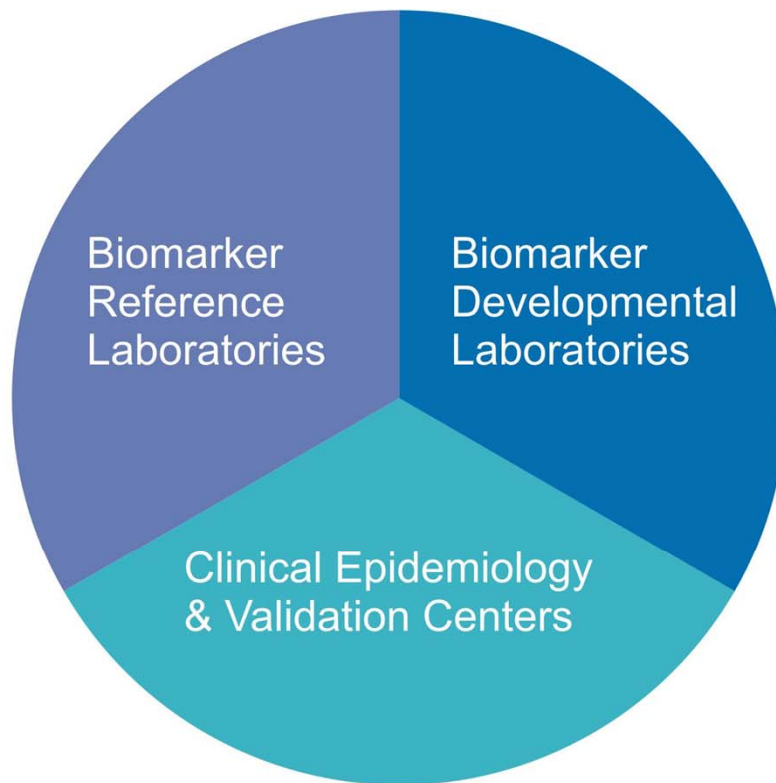
**Division of Cancer Prevention**

**March 2, 2009**



# INVESTIGATOR-DRIVEN CONSORTIUM

Early  
Detection  
Research  
Network 



***An “infrastructure”  
to support  
collaborative  
research on  
molecular, genetic &  
other biomarkers in  
human cancer  
detection & risk  
assessment***



## Implement biomarker research through:

- **systematic, evidence-based discovery**
- **development & validation of biomarkers for cancer risk, early detection, diagnosis & prognosis of cancer**

# REVIEW OF EDRN BY EXTERNAL COMMITTEES

## EDRN External Review Committee, February 2007

**Chair: Dr. Bernard Levin**

**Members:**

**Dr. Ken Cowan**

**Dr. Arnie Kaluzny**

**Dr. Barnett S. Kramer**

**Dr. Brian Reid**

# REVIEW OF EDRN BY EXTERNAL COMMITTEES

## EDRN Working Group, November 2008

**Chair: Dr. Hal Moses**

**Members:**

**Dr. J. Carl Barrett**

**Dr. Paul Engstrom**

**Dr. Sam Gambhir**

**Dr. Jim Heath**

**Dr. John Mendelsohn**

**Dr. John Minna**

**Dr. Jean Wang**

# REPORTS OF REVIEW COMMITTEES

- **EDRN's present structure & process supports its mission**
- **Quality & number of publications (>560) & validation projects (>15) were praised**
- **The Working Group suggested:**
  - term of chairmanship
  - establishment of BSA subcommittee as advisors
  - empowering Steering Committee as the governance body
  - enhancing communication
- **Committees' recommendations will be implemented.**

# COMPETITIVE RENEWAL

Early  
Detection  
Research  
Network 

**To begin in March 2010**

# MAINTAINING THE INFRASTRUCTURE, EXPERTISE & RESOURCES

- **Key NCI program to develop & validate biomarkers**
- **Over 127 scientific advances**
- **Over 15 validation studies**
- **Rigorous process for biomarker discovery & validation for definitive population testing**
- **Supports integrated biomarker research**



# BEST BUSINESS PRACTICES

## **Often Cited for Best Practices for Milestones Driven Project Management:**

- **Informatics for Biomarker Research (NCI-FDA-AACR Biomarker Collaborative Working Group Reports, Institute of Medicine)**
- **Discovery & Validation Research (JNCI 2006, J. Proteome Research 2008)**
- **Collaborative Model for Biomarker Research (Nature 2008); Other NIH program have adopted EDRN's business model**
- **NCI Translational Research Working Group (Clinical Cancer Research 2008); Proposed TRWG's STRAP program is inspired by EDRN Core Fund Concept**

# EDRN AS A CATALYST

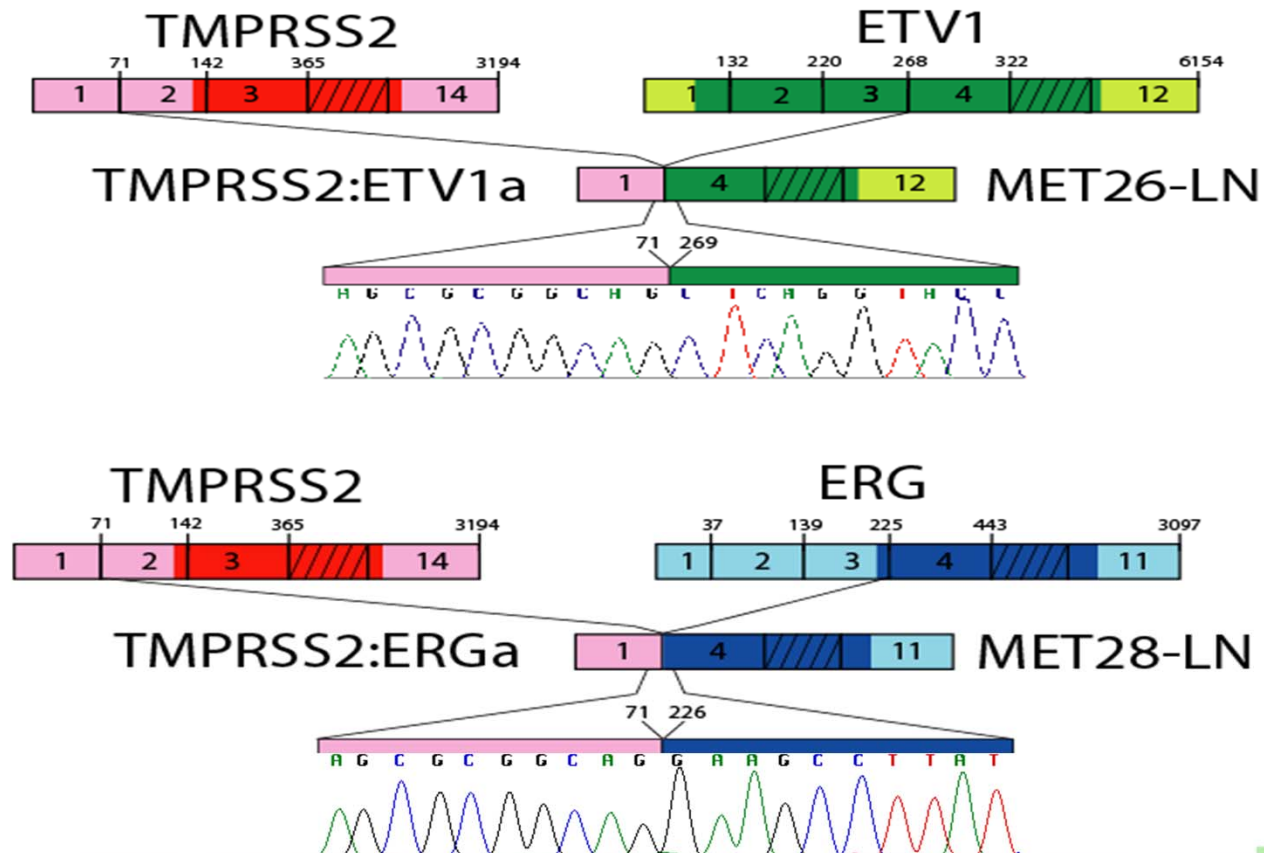
- **Partnerships (MOUs) with foundations: Canary on prostate & lung; Lustgarten on pancreatic cancer**
- **Biotechnology & Diagnostics Companies – see EDRN as a standard model & work with EDRN investigators**
- **Incubator projects with private sector, e.g., platform validation with MesoScale, reagents with SourceMDx, miRNA array with Agilent**
- **International collaborations with Australia & Turkey (mesothelioma), India (oral cancer), All Ireland-NCI (colon), Italian EDRN (multiple tumors)**
- **Collaboration with AACCC & ASCO on clinical test standards; with HUPO on validation**
- **Collaboration with NCI's: SPORE, PLCO, MMHC, & Clinical Proteomics**

# DISCOVERY OF GENE FUSION IN PROSTATE CANCER

Early  
Detection  
Research  
Network 

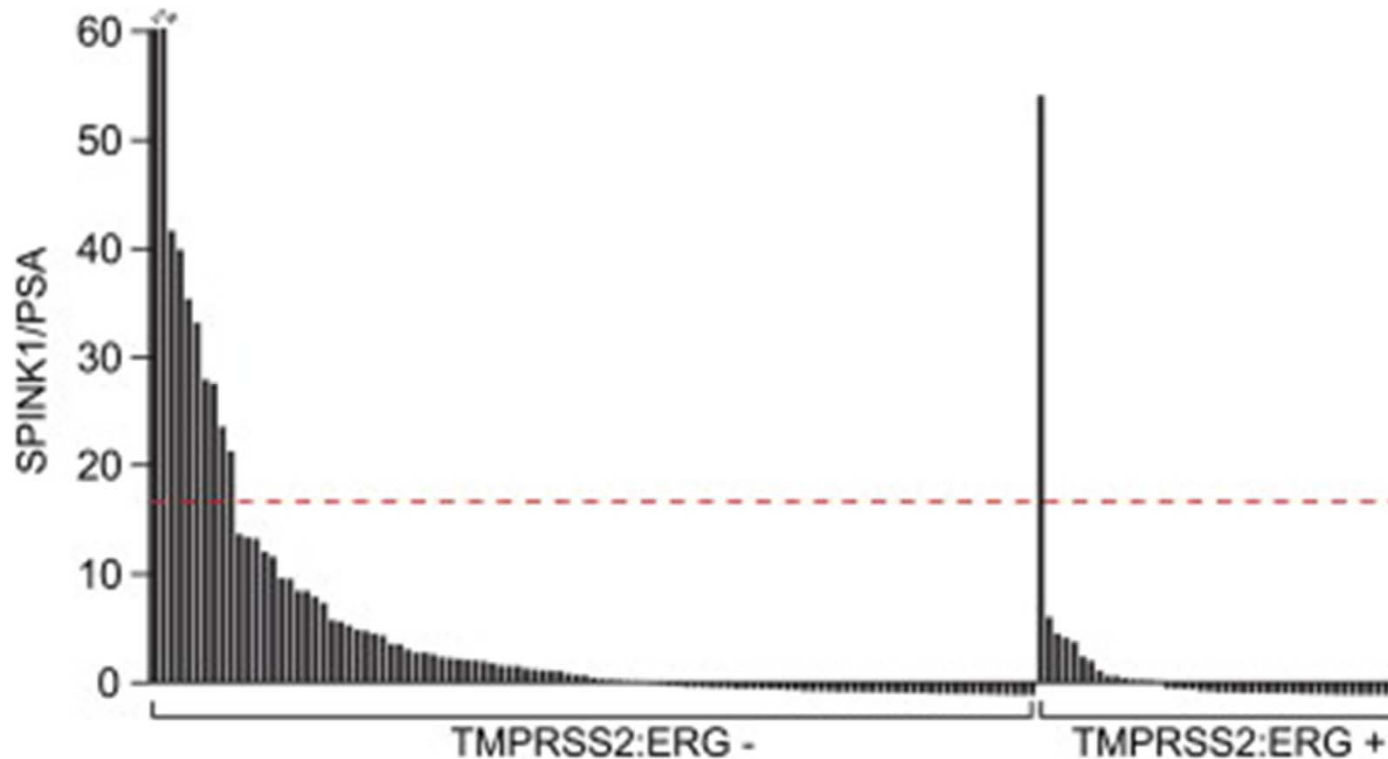


**Recurrent Fusion of TMPRSS2 and ETS  
Transcription Factor Genes in Prostate Cancer**  
Scott A. Tomlins, *et al.*  
*Science* 310, 644 (2005);



### The Role of *SPINK1* in *ETS* Rearrangement-Negative Prostate Cancers

*SPINK1* Outlier Expression Can Be Detected Non-invasively in Urine



# DISCOVERY TO EARLY CLINICAL TESTS

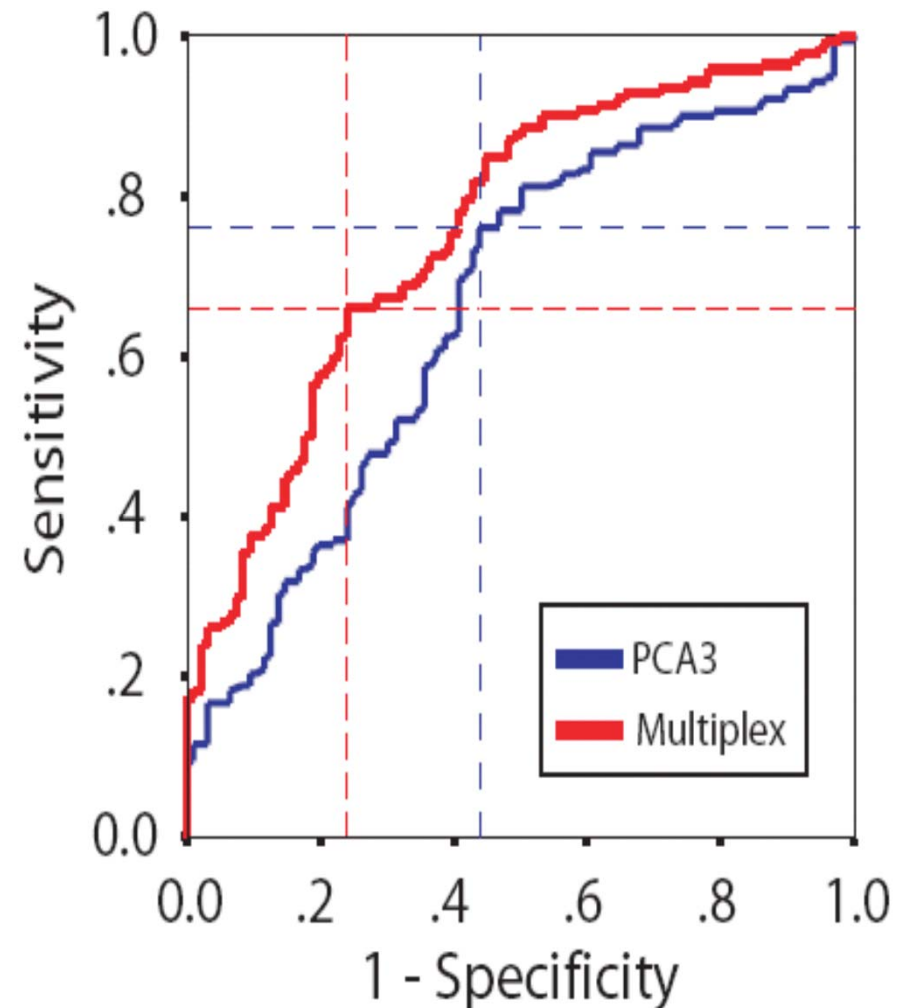
## A First-Generation Multiplex Biomarker Analysis of Urine for the Early Detection of Prostate Cancer

### Multiplex Urine Test for Prostate Cancer (TMPRSS2-ERG + SPINK1 + PCA3 + GOLPH2)

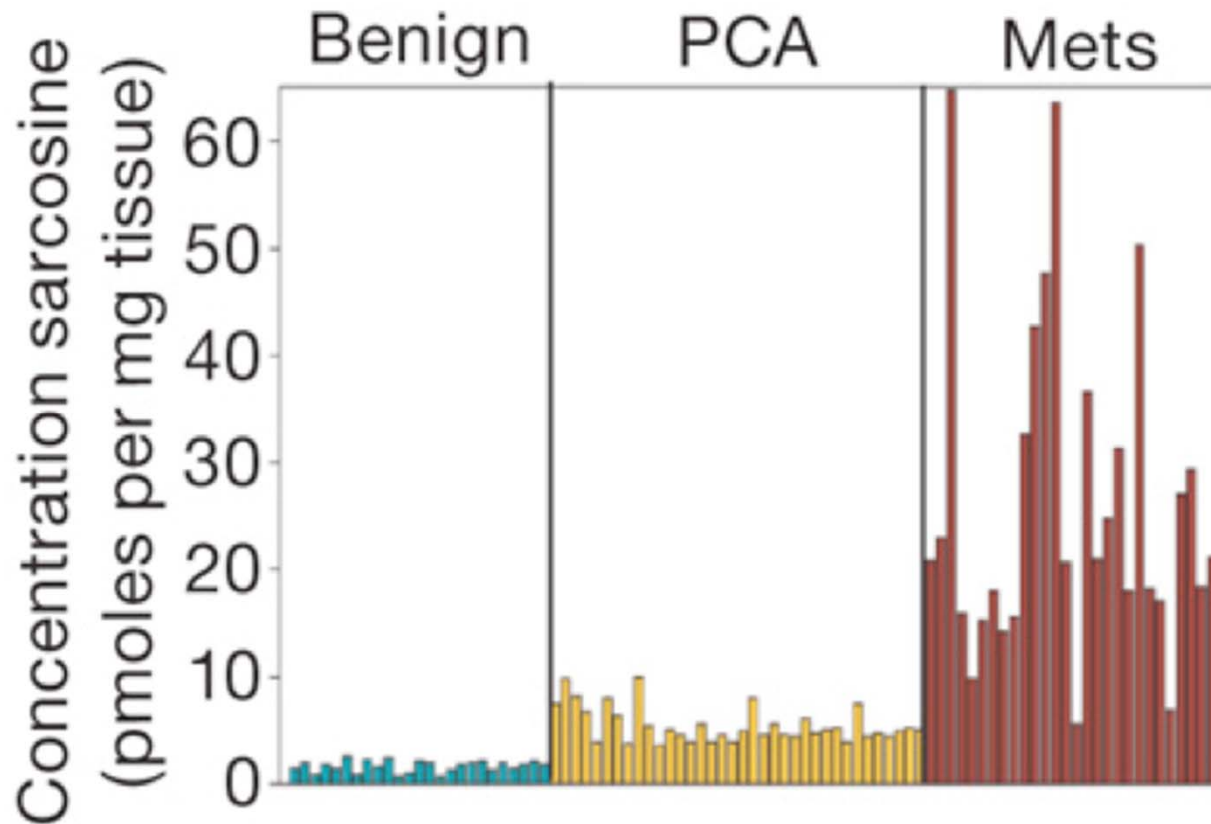
n=234

Approx. 70% Sens/spec  
In high PSA older men (PSA>4.0)  
Bx Positive vs. Bx. Negative

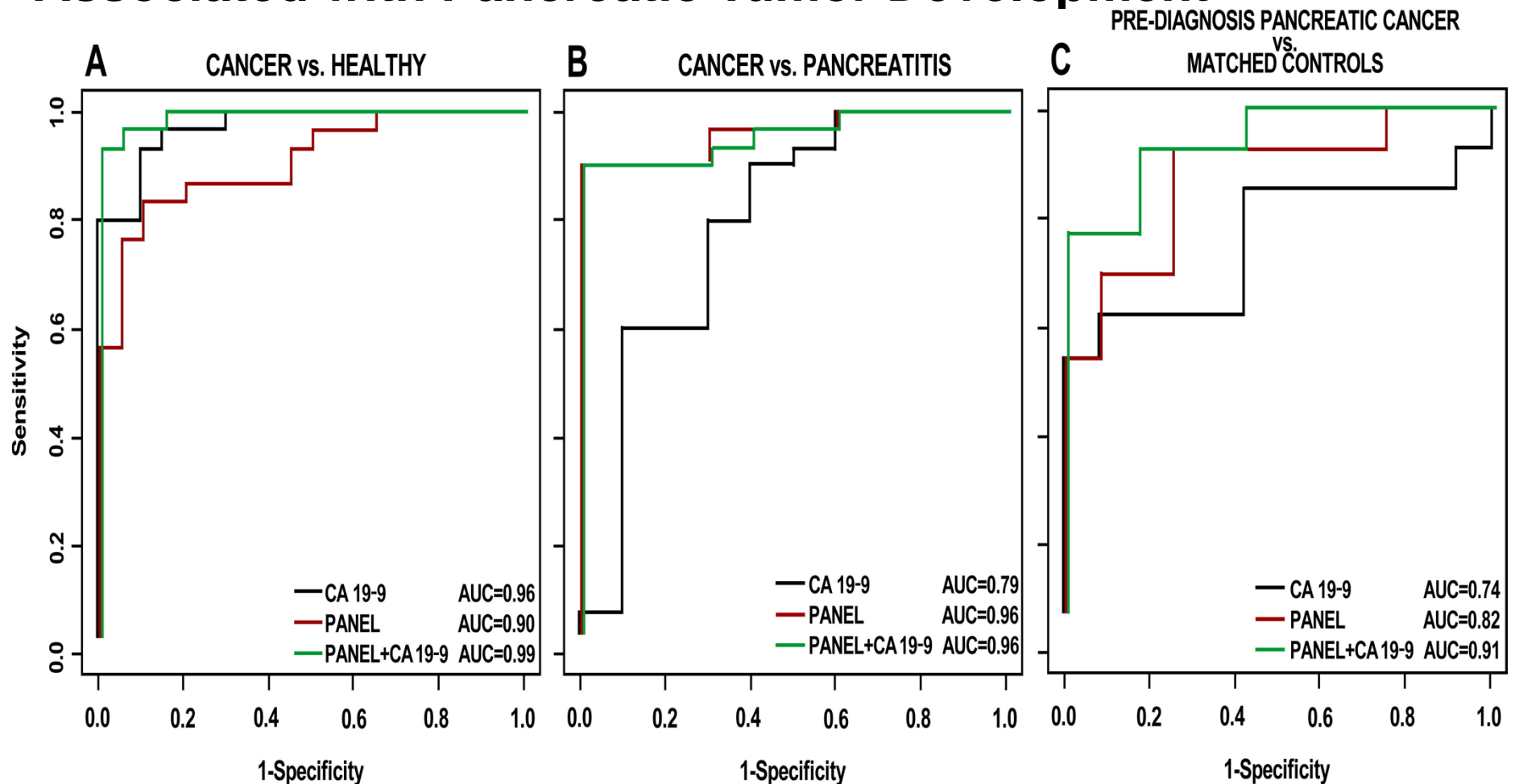
AUC 0.76



## Metabolomic Profiles Delineate Potential Role for Sarcosine in Prostate Cancer Progression

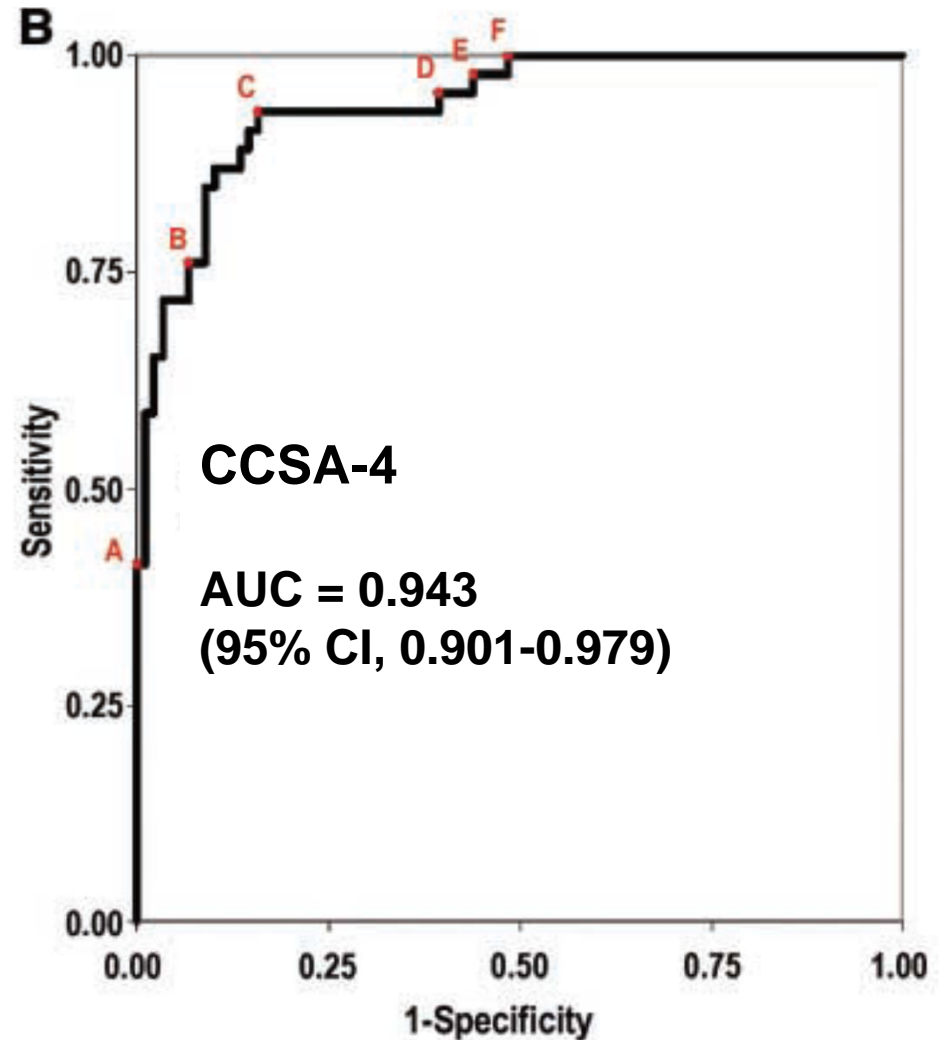
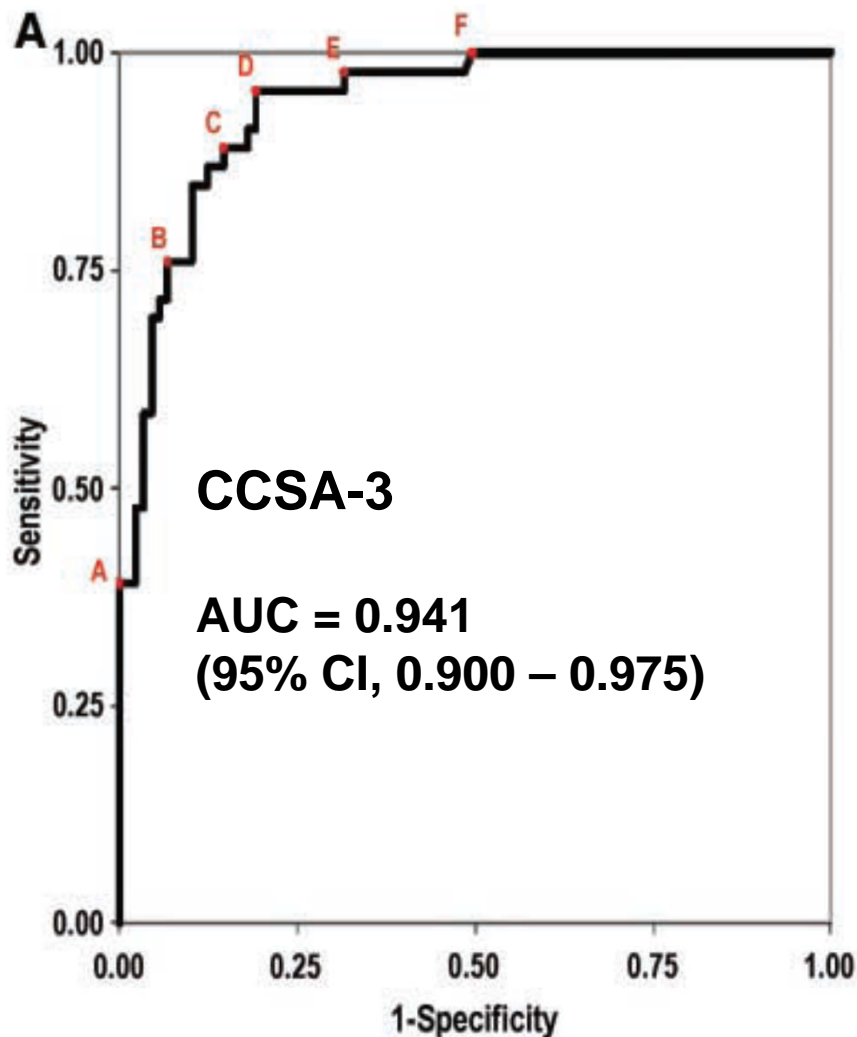


## A Mouse to Human Search for Plasma Proteome Changes Associated with Pancreatic Tumor Development



# DISCOVERY TO EARLY CLINICAL TESTS

## Initial Analyses of Colon Cancer–Specific Antigen (CCSA)-3 and CCSA-4 as Colorectal Cancer–Associated Serum Markers





## **Moving biomarkers from discovery to pre-validation (*credentialing*) to validation (*creation of modality*)**

- **Over 127 biomarkers in Phase 1 & 2**
- **Over 15 validation studies in Phase 2-3 pipeline**
- **Five biomarkers in Phase 3**
- **Over 27 Patents & 17 Licenses**

# MULTI-INSTITUTIONAL CLINICAL VALIDATION STUDIES/TRIALS

Completed and Continuing

Early  
Detection  
Research  
Network 

- **Bladder cancer – MSA (PI: Mark Schoenberg)**
- **Colorectal cancer – Novel serum-based markers, CCSA-3 & CCSA-4, (PI: Robert Getzenberg)**
- **Esophageal cancer – Methylation Panel (PI: Steve Meltzer)**
- **Liver cancer – DCP & AFP-alpha 3 (PI: Jorge Marrero)**
- **Lung cancer – Annexin 1 & Annexin 2, Theta (PI: Samir Hanash)**
- **Mesothelioma – Serum Mesothelin Related-Proteins (SMRP) & Osteopontin (PI: Harvey Pass)**
- **Ovarian Cancer Biomarker Validation (EDRN PI: Dan Cramer, PI: SPORE, Nicole Urban, Yale & LabCorp, PI: Gil Mor)**
- **Prostate cancer – percent proPSA as a marker to improve negative predictive value (EDRN/Beckman-Coulter multi-institutional study, PI: Dan Chan)**
- **Prostate cancer serum-based proteomics (PI: John Semmes)**

# NEW COLLABORATIVE OPPORTUNITIES IN REISSUANCE

- **Collaborate with SWOG & CALGB on joint-review of biomarker-related clinical trials to add EDRN biomarkers for validation**
- **Establish database to capture & share methods for validation & qualification of biomarkers (recommended by BSA WG)**
- **Integrate genetic, cell signaling & biochemical pathways with biomarker discovery**
- **Collaborate with NCI's CISNET to employ cost-effectiveness approaches to evaluate biomarker discovery, development & validation**
- **Collaborate with The Cancer Genome Atlas**

# BUDGET FY 2010 - 2015

- **The requested budget is \$32 M/year**
  - Biomarker Development Laboratories: \$10 M**
  - Clinical Epidemiology and Validation Centers: \$10 M**
  - Biomarker Reference Laboratories: \$3 M**
  - Data Management & Coordinating Centers \$3 M**
  - Core Fund: \$6 M**
- **42 institutions; more than 300 investigators; lowest cost per grant for an infrastructure-related program;**
- **The Core Fund is essential to rapidly move biomarkers into validation trials. The average cost of a multi-year validation trial is \$3 M - \$4 M. All phase III studies/trials are conducted using Core Fund.**

**Thank you**