Reissuance Request

Peter Greenwald, MD, DrPH
Sudhir Srivastava, PhD, MPH
Division of Cancer Prevention
March 2, 2009
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
• 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

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
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 AACC & 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

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

TMPRSS2:ETV1a

MET26-LN

TMPRSS2

ERG

TMPRSS2:ERGa

MET28-LN
The Role of *SPINK1* in *ETS* Rearrangement-Negative Prostate Cancers

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

CCSA-3
AUC = 0.941
(95% CI, 0.900 – 0.975)

CCSA-4
AUC = 0.943
(95% CI, 0.901-0.979)

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

- 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
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