

**Early
Detection
Research
Network**



**Early Detection Research Network (EDRN)
A National Infrastructure
for Biomarker Development**

*Pre-Application Meeting
December 2, 2014*

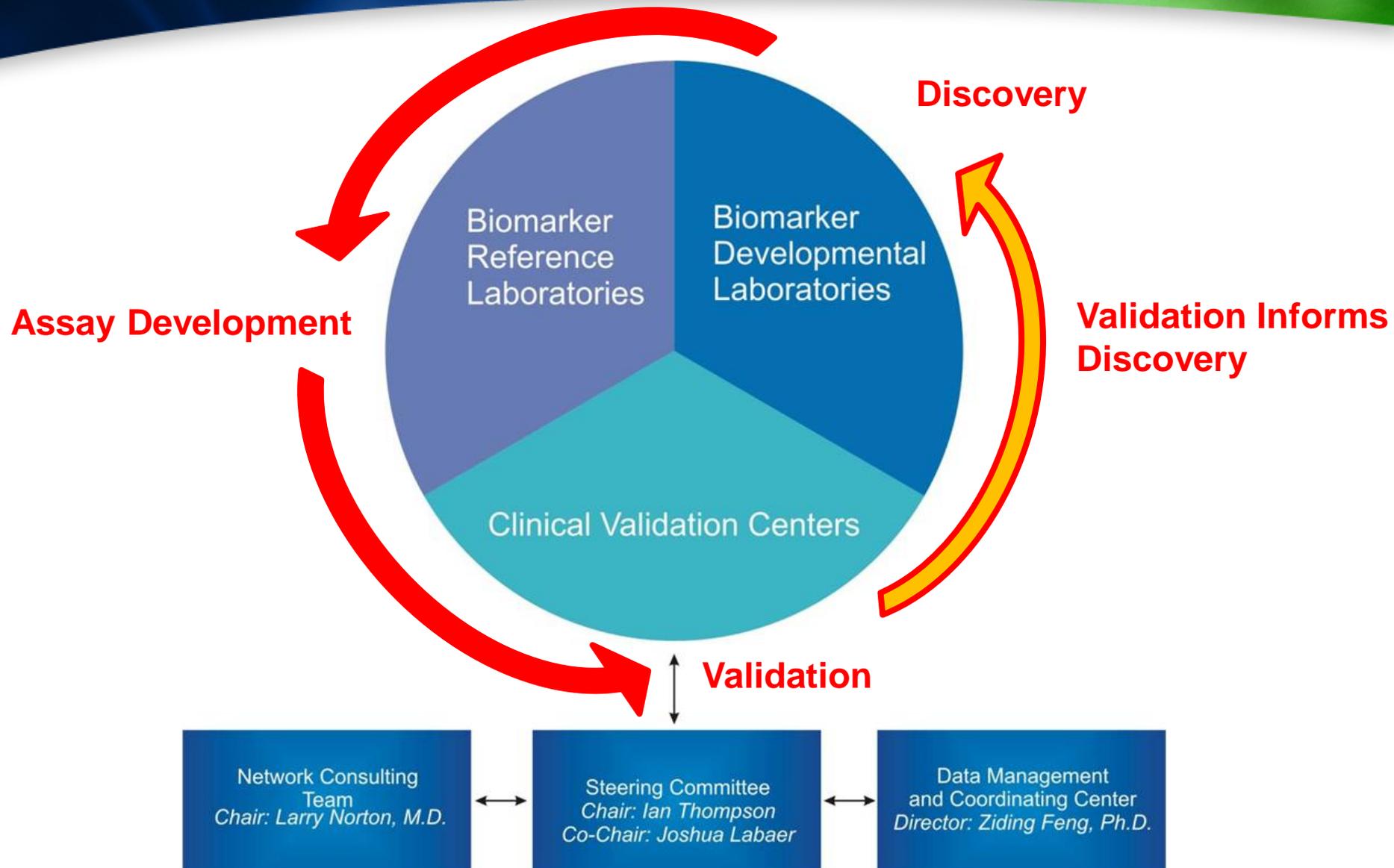
**Sudhir Srivastava, Ph.D., MPH
Chief, Cancer Biomarkers Research Group**



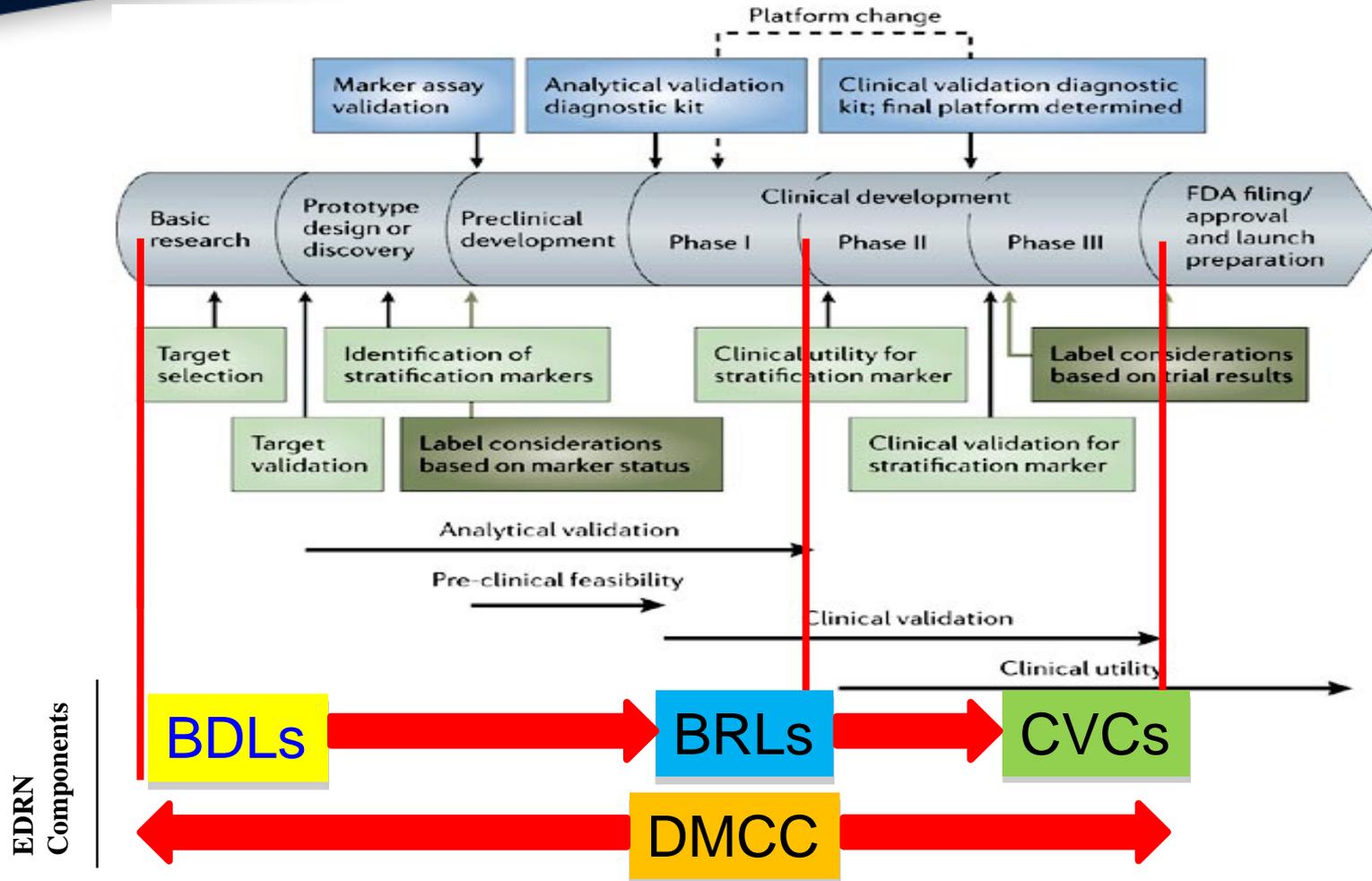
EDRN Program Objectives

- **Establish an investigator-initiated infrastructure to support development and validation of early detection biomarkers and markers of progression**
- **Foster interaction between academic, clinical and industrial leaders**
- **Standardize biomarker validation criteria**
- **Develop a quality assurance program**
- **Bring biomarkers to clinical use**

Organization of EDRN



EDRN Biomarker Pipeline: Modeled After Drug Discovery Pipeline



BDLs= Biomarker Developmental Labs; BRLs= Biomarker Reference Labs; CVCs = Clinical Validation Centers; DMCC = Data Management and Coordinating Center.

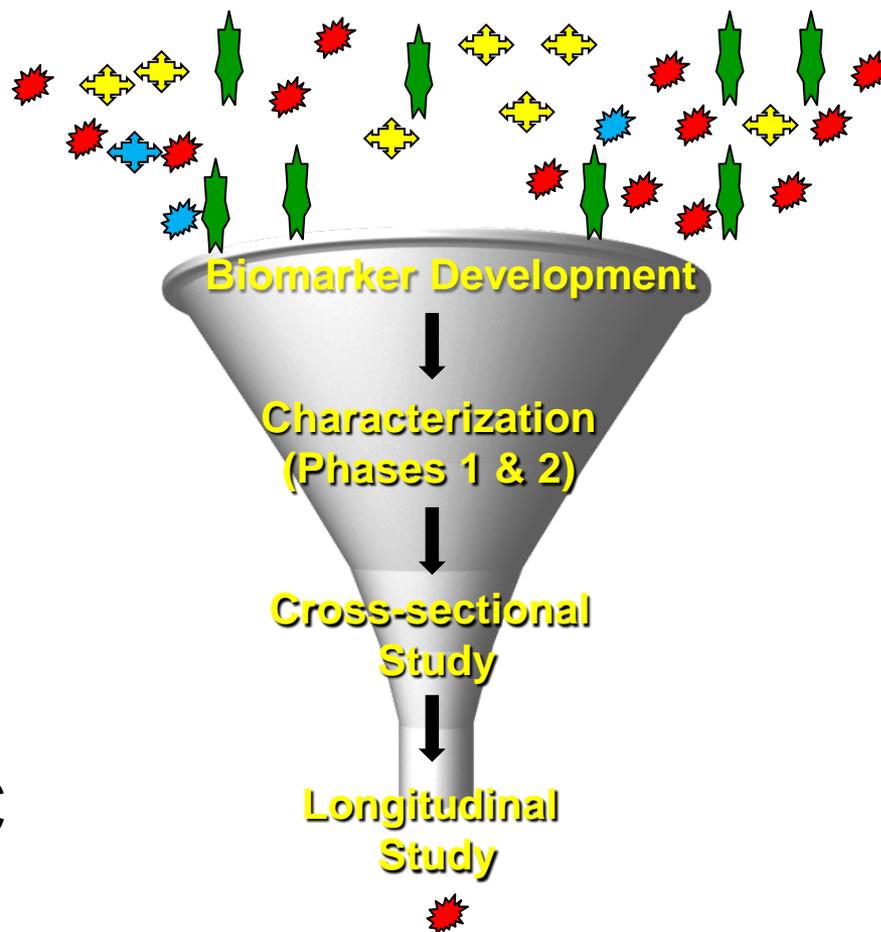
Biomarker Triage System in EDRN

BDL

BRL

CVC

DMCC



Discovery

Markers from
both EDRN and
other researchers

Scientific Accomplishments

Study Designs for Biomarker Development

Phases of Biomarker Discovery and Validation

**PRoBE
Study
Design:**
Prospective-
Specimen-
Collection,
Retrospective
e-Blinded-
Evaluation

<i>Preclinical Exploratory</i>	PHASE 1	<i>Promising directions identified</i>
<i>Clinical Assay and Validation</i>	PHASE 2	<i>Clinical assay detects established disease</i>
<i>Retrospective Longitudinal</i>	PHASE 3	<i>Biomarker detects preclinical disease and a "screen positive" rule defined</i>
<i>Prospective Screening</i>	PHASE 4	<i>Extent and characteristics of disease detected by the test and the false referral rate are identified</i>
<i>Cancer Control</i>	PHASE 5	<i>Impact of screening on reducing burden of disease on population is quantified</i>

Phases of Biomarker Development for Early Detection of Cancer

Margaret Sullivan Pepe et al.

J Natl Cancer Inst, Vol. 93, No. 14, July 18,
2001

Pivotal Evaluation of the Accuracy of a Biomarker Used for Classification or Prediction: Standards for Study Design

Margaret Sullivan Pepe et al.

J Natl Cancer Inst 2008; 100:1432-1438

Partnering Organizations



- National Institute of Standards and Technology
- Center for Prostate Disease Research, DOD
- Pacific Northwest National Laboratory, DOE
- Jet Propulsion Laboratory, NASA
- Canary Foundation of America
- Lustgarten Foundation N.Y.
- International collaborations:
China (C-EDRN), Cancer Research-UK, Turkey, Japan, Chile, Israel
- Industry (15 active)
- Associate Members (more than 200)

Strategic Partnerships

- Precompetitive data sharing (e.g., proPSA with **Beckman Coulter**, PCA3 with **GenProbe**)
- Leveraging Resources
 - **Canary, Inc.** uses EDRN Data management system for lung and prostate markers
 - **Lustgarten Inc.** funded 20-hybridoma cell lines for pancreatic candidate markers
- International Partnerships
 - **Turkey, Chile** (mesothelioma)
 - **China** (HCC, lung)
 - **Cancer Research UK** (pancreatic, lung)
 - **EU** European Advanced Translational Research Infrastructure (www.eatris.eu)

Salient Features of EDRN

- Provide **Integrated Infrastructure**
- **Build Resources** for Biomarker Research
- **Establish Standardized Criteria** for Biomarker Discovery and Validation
- **Quality Assurance** Programs
- Ensure Research **Reproducibility**
- Improve Screening and Diagnostic **Tests for Common Clinical Dilemmas**

EDRN Milestones: From Structure to Process to Outcomes

2000-2005 Coordinate, Communicate and Collaborate	2005-2010 Learn, Improve and Deliver	2010-Present Productivity, Outcome and Dissemination
<ul style="list-style-type: none"> ✓ 33 Principal Investigators ✓ Steering Committee Attendance: 85; Workshop 300 ✓ Associate Membership Program Initiated; 32 Associate Members ✓ <u>EDRN-Gordon Research Tie-up (2002, 2003)</u> ✓ Initiated EDRN-Human Proteome Organization Plasma Proteome Project ✓ <u>Guidelines for Biomarker Discovery and Validation</u> ✓ Project Management Tools Created ✓ <u>Multi-center Trial Informatics Infrastructure created, verified</u> ✓ <u>Virtual Specimen Bank Established</u> ✓ <u>IRB Approvals Monitored: 38 sites</u> 	<ul style="list-style-type: none"> ✓ 45 Principal Investigators ✓ Steering Committee Attendance: 120; Workshop 300 ✓ 123 Associate Members ✓ 2 EDRN-Gordon Research Workshops (2005, 2007) ✓ <u>MOUs signed With Canary Foundation, Lustgarten Foundations, Turkey</u> ✓ <u>OVA1 FDA Approved</u> ✓ <u>EDRN-FDA Educational Biennial Workshop</u> ✓ EDRN-NIST Workshop on Standards ✓ <u>IRB approvals monitored: About 80 sites</u> 	<ul style="list-style-type: none"> ✓ 57 Principal Investigators ✓ Steering Committee Attendance: 150; Workshop: 350 ✓ 231 Associate Members ✓ <u>DCP and AFP-L3 FDA Approved for Liver Cancer and ROMA for Ovarian Cancer</u> ✓ <u>proPSA and PCA-3 FDA Approved for Prostate Cancer</u> ✓ <u>11 CLIA-approved Diagnostic Tests</u> ✓ <u>10 Clinical Reference Sets completed and stored at Frederick, MD</u> ✓ <u>IRB Approvals Monitored: 216; 200 Protocols;100 MTAs</u>

Integrated Infrastructure (BDLs, BRLs, CVCs, DMCC)

- **Vertically integrated infrastructure for discovery, development and validation of biomarkers:**
 - >200 active protocols; >100 MTAs and IRBs
 - >800 candidate biomarkers prioritized for evaluation;
 - ~300 moved forward to Phase 2 and Phase 3 validation
 - >10,000 subjects enrolled
 - >12 clinical validation studies
- **Policy and Procedures in place for transparency and effective management**
- **Effective hand-off mechanism from BDL to BRL to CVC**

EDRN cited as a model organization (best practices for project management driven by milestones and operational guidelines, manual of operations, and team approach) by AACR, NCI Translational Research Working Group, IOM, Nature, Science, J. Proteome Research.

“The EDRN [process]...helps the field to avoid numerous competing claims of being ‘the biomarker of choice’, the notion of which arises simply from marketplace competition or differences between laboratories.

The EDRN approach facilitates well-designed clinical studies that have an **increasing hierarchy of complexity.**”

Building Resources for Clinical Studies

- Platform for multi-center biomarker validation studies
- CLIA-approved laboratories to develop and test assays using GLP and GMP
- Centralized statistical center for data analysis and informatics infrastructure to share data
- Mechanism for biomarker triaging prior to large, expensive validation studies (use of Reference Sets)
- > 100,000 clinically-annotated biospecimens using common data elements (CDEs)

Building Resources for Clinical Studies: Standard Biospecimen Reference Sets

Housed at Frederick National Laboratory

- **Bladder**
- **Breast**
- **Colon**
- **Lung**
- **Liver**
- **Pancreas**
- **Prostate**
- **Ovary**

<http://edrn.nci.nih.gov/resources/sample-reference-sets>



Building Resources for Clinical Studies: Informatics and Bioinformatics (Jet Propulsion Lab)

- VSIMS for multicenter validation studies
- eSIS for study management
- ERNIE for Virtual Specimen Banks established (tracks >100,000 biospecimens)
- Prioritized Biomarker Database
- >2600 Common Data Elements
- Validation data collected through LabCAS (proteomic and genomic data) and eCAS
- Crowd-sourcing being considered on stored data

Basic VSIMS Instance

Directory, mailing lists, data transfer, protocol and IRB information.

Completed for:

- SSD
- Lung Cancer
- Breast's Biobank
- ESDN/WH Colon
- Mesothelioma
- Ovarian/PAO
- Ovarian/PUCO
- proPSA
- Canary Never Smokers
- Canary TMA
- Breast Ref
- DCP & Liver Ref
- Lung Ref
- Pancreatic Ref
- Prostate Ref
- Colon Ref
- Cancer in Women Ref
- MSA & Stool Ref
- PCAS & Prostate Ref
- Tropic Nucleic Acid
- Canary PASS
- Bone & Breast Disease (BBD)
- DCIS
- Pancreatic Cyst Ref
- Bulk OES Colon
- Lung Nodule
- H205

Ongoing Challenges:

- Extra Programming Required
- Common Code vs. Customized Code

Specimen Monitoring & Selection

Create data table that combine data from our systems with specimen storage data from NCI Fredrick.

Specimen selection includes:

- monitoring specimens at NCI Fredrick, requesting data modifications as needed
- selecting specimen sets to send for analysis
- documenting analyst-specific information (lab specimen IDs, blinded subject IDs, etc.)
- documenting where each specimen is and how it is used

Ongoing Challenges:

- Data quality control involves both NCI Fredrick and the DMCC
- Labs altering the Specimen IDs (truncating)

Eligibility Programming

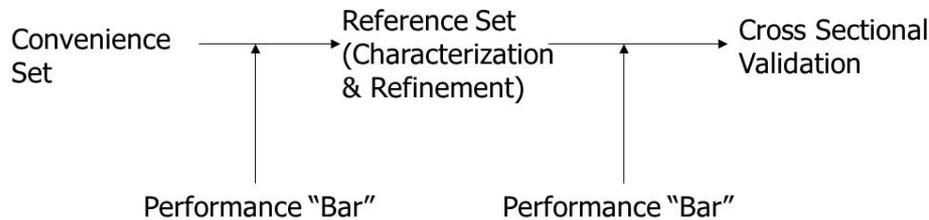
Translated the protocol language into data elements and programming. Create Eligibility Flow Chart. Allow us to verify that all the CDEs necessary to create eligibility have been included in the form, and that the logic works to identify eligible participants.

Ongoing Challenges:

- Eligibility is complex
- Some protocols can be very complex
- Some protocols require changes when there are new CDEs and the programming

Scientific Accomplishments: Decision Criteria for Biomarker Triaging

Example: Colon Cancer



Performance in Reference Set
without FOBT:

TPR $\geq 33\%$ $(TP/TP+FN)$
FPR $\leq 30\%$ $(1 - (TN/TN+FP))$

Rationale:

1. If more accessible biosample other than stool, might enhance screening adherence.
2. May justify equivalent performance to FOBT

Performance in Reference Set+FOBT:

TPR $\geq 70\%$ $(TP/TP+FN)$
FPR $\leq 30\%$ $(1 - (TN/TN+FP))$

Rationale:

1. Must beat best current standard (FOBT, now fecal immunochem by at least 20%)
2. FPR less important as FP will get colonoscopy in any event.

Decision Rules

Biomarker	TPR	FPR
Galectin-3 ligand	72%	20%
Vimentin Methylation	83%	15%
K-ras in Urine	77%	35%
K-ras FOBT card	14%	35%
GOS	77%	51%
GOS +FOBT	27%	5%
Proteomics-Agilent	78%	12%
Proteomics-PBSIIc	70%	24%
Proteomics-SELDI-TOF	19%	2%
Proteomics-MALDI-TOF	63%	52%
p53	40%	30%
CEA	40%	30%
Topoisomerase II	35%	30%
Cathepsin D	50%	30%
Cyclin B	40%	30%
IGF Binding Protein 2	35%	30%
TRAILR2 (diaDexus)	10%	4%
CIN248 (diaDexus)	12%	8%
P108 (diaDexus)	27%	6%
Three diaDexus Alone	29%	40%
Three diaDexus+FOBT	42%	3%

**Rapid Biomarker Screening
in Reference Sets**

Scientific Accomplishments

> 900 Verified Biomarkers in the Pipeline

- Vimentin methylation in stool as a biomarker of advanced adenoma ([Sandy Markowitz](#))
- TMPRSS2-ERG (T2-ERG) fusion for detection of aggressive prostate cancer ([Arul Chinnaiyan](#))
- 80-gene panel for lung cancer detection now being verified for application in nasal epithelium ([Avrum Spira](#))
- Circulating DNA for colon, ovary and endometrial cancer ([Ken Kinzler/Bert Vogelstein](#))

>1900 publications; ~22% in journals with impact factor ≥ 7

Completed Validation Studies

Five FDA Approved Diagnostic Tests

Biomarker	Clinical Utility	Year of Approval	EDRN PI/ Industrial Partner
%[-2]proPSA	<u>Reduce the number of unnecessary initial biopsies.</u> Also, appears to be highly associated with increased risk of aggressive disease.	2012	Dan Chan/ Beckman Coulter
PCA3 (in urine)	<u>Repeat biopsy decisions</u> in patients at risk for prostate cancer.	2012	John Wei/ Gen-Probe
OVA1™ (5 analytes: CA 125, prealbumin, apolipoprotein A-1, beta2 microglobulin, transferrin)	<u>Prediction of ovarian cancer risk</u> in women with adnexal mass.	2010	Dan Chan/ Vermillion
Risk of Ovarian Malignancy (ROMA) algorithm with CA125 and HE4 blood tests for pelvic mass malignancies	<u>Prediction of ovarian cancer risk</u> in women with pelvic mass.	2011	Steve Skates/ Fujirebio Diagnostics
DCP and AFP-L3 combined panel of markers	<u>Risk assessment</u> for development of hepatocellular carcinoma.	2011	Jorge Marrero/ Wako Diagnostics (> 1 million sold)

Eleven CLIA (Clinical Lab Improvements Amendments) Certified Diagnostic Tests

Biomarker Assay	Purpose	PI/CLIA Laboratory
MiPS (Mi Prostate Score Urine test), Multiplex analysis of T2-ERG gene fusion, PCA3 and serum PSA	Detection of prostate cancer	A. Chinnaiyan/Gen-Probe
IHC and FISH for T2-ERG fusion	Detection of prostate cancer	A. Chinnaiyan/Roche
GSTP1 methylation	Repeat biopsies in prostate cancer	D. Sidransky/OncoMethylome
Mitochondrial deletion	Detection of prostate cancer	NIST/Mitomics
Proteomic panel	Detection of lung cancer	W. Rom/Celera
Aptamer-based markers	Detection of lung cancer	W. Rom/Somalogic
80-gene panel	Detection of lung cancer	A. Spira/Allegro
Vimentin methylation in stool	Detection of colon cancer	S. Markowitz/LabCorp
Galectin-3 ligand	Detection of advanced adenomas and colon cancer	R. Bresalier/BG Medicine
GP73	Risk of hepatocellular carcinoma	T. Block/Beckman Coulter
8-gene Panel for Barrett's Esophagus	Progression Prediction of BE	Stephen Meltzer//Diagnovus

Scientific Accomplishments

Ongoing and Planned Studies: Examples

Ongoing: >12 studies

- DNA methylation and Galectin-3 ligand, and DNA markers for advanced adenoma and [colon cancer](#) detection (D. Brenner; Exact Sciences)
- SMRP and Fibulin-3 in [mesothelioma](#) (H. Pass; Chile)
- T2-ERG fusion and PCA3 score combined for detection of aggressive [prostate cancer](#) (Martin Sanda)
- Molecular biomarkers in airway and blood for detection of early stage lung cancer in indeterminate nodules (in collaboration with DOD)
- Hepatocellular Carcinoma Early Detection Strategy: biomarkers in detecting preclinical HCC

Planned: >15 studies

- [PHI \(pro-PSA\) and PCA3 for improved prostate cancer detection](#)
- [SCHLAP1 \(non-coding RNA\) and SPOP](#) in urine to complement PCA3/T2-ERG
- Biomarkers for prostate cancer progression among patients on [Active Surveillance](#)
- Partial wave spectroscopic [PWS] microscopy for screening for colorectal cancer and advanced adenoma
- Circulating ovarian cancer biomarkers in PLCO and UKCTOCS prediagnostic biospecimens

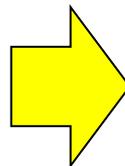
Adapting to Changing Landscape of Biomarker Science

- Focus on indeterminate nodules identified by screening lung CT (25% of subjects in National Lung Screening Trial)
- Changing regulatory requirements for biomarker qualifications (FDA)
- Responding to regulatory needs, e.g., a laboratory selected for e-cigarette evaluation
- Response to congressional directives on 'recalcitrant cancers', e.g. pancreas, liver and lung
- Focus on developing biomarkers for overdiagnosed cancers such as breast, prostate

Does the Total Exceed Sum of Its Parts?

THEN (Prior to 2000)

- No SOPs for biosamples, reagents, methodologies, etc.
- No common data elements (data dictionary) to enable the development of common databases for biosample annotation
- Fragmented studies with convenience samples, not generalizable



NOW

- Network of integrated resources for supporting validation
- Checks and balances ensure good biomarkers are promoted without regard to pecuniary interests
- Provides infrastructure for promising markers to become medical tools
- Standard operating procedures for biosample collection and management.
- Developed roadmap for study designs for clinical verification and validation
- EDRN activities are not replicated within industry or academia

Highlights of FOAs

- Biomarker Developmental Laboratories ([RFA-CA-14-014 U01](#))
- Biomarker Reference Laboratories ([RFA-CA-14-016 U24](#))
- Clinical Validation Centers ([RFA-CA-14-015 U01](#))
- Data Management and Coordinating Center ([RFA-CA-14-017 U24](#))

All of these FOAs are funded through the Cooperative Agreement Mechanisms in which there is substantial involvement of NCI staff

General Requirements Pertaining to all FOAs

- Adhere to FOA-specific scope, specific requirements, page limitations, and other details;
- Describe study designs
- Describe statistical analyses
- Collaborate with Cohort Consortia, HMOs, Cooperative Groups, and other relevant entities for “shovel-ready” biospecimen collections
- Pay attention to review criteria when preparing your application
- Describe licensing and IP management plan, if applicable.

Biomarker Developmental Laboratories: Expectations

- Investigators with extensive laboratory skills and experience with biomarker research
- Experience with knowledge and principles of biomarker discovery, e.g., EDRN's 5-phase criteria, PRoBE Design and any other acceptable guidelines
- Availability of quality specimens for discovery as opposed to “convenience samples”
- Statistical analysis plan for multiplicity and minimizing false-discovery rate, e.g., multiple platforms, multiple biomarkers, plan for avoiding chance, bias, over-fitting, etc.
- Biomarkers addressing a specific question(s) in the realm of early detection (Phase 1 and Phase 2)

Biomarker Developmental Laboratory: Expectations

- Integrated 'Omic' approaches with imaging (whenever feasible) to provide specificity and sensitivity
- Decision criteria for triaging candidate biomarkers for a given clinical application
- Achievable timeline of proposed research
- Collaboration to complement expertise and resources
- IP and licensing plan to ensure that collaboration is not affected

Biomarker Reference Laboratory: Expectations

- Experience with GLP/CLIA/CAP practice and principles
- Experience with laboratory medicine
- Collaboration with diagnostic/biotech/industrial scientists for clinical grade assays and scale-up
- Provide a clear assay development pipeline for markers meeting EDRN Phase 2 criteria
- Ability to create CLIA-compliant assay protocols, conduct assay for EDRN validation studies and laboratory resources in one or more “Omic” technologies
- Achievable time-line for the project period with decision criteria for triaging assays and technology

Clinical Validation Center: Expectations

- Patient populations and resources for conducting multi-institute, multi-discipline clinical validation studies
- Sound knowledge and expertise in principles and practices for conducting clinical trials
- Partnerships with Cooperative Groups, HMOs, Cohort Consortia for accessing and collecting specimens without any need for infrastructural support
- Supportable clinical questions on early detection and/or related issues with decision criteria for inclusion of proposed biomarker panel
- Achievable timeline for proposed study to be completed in 5 years with a provision of an interim analysis in year 3/4

Data Management and Coordinating Center: Expectations

- Demonstrate experience in managing complex biomedical consortia, networks, or equivalent entities with multi-discipline, multi-site activities
- Ability to manage, improve, maintain laboratory management systems (like VSIMS) for conducting multi-center trials
- Strong background and experience in statistical study designs, protocol management, informatics, BIG data
- Ability to maintain confidential communication on patient data (storage, retrieval, dissemination) through Web Portal, Secure Website, etc.
- Ability to coordinate meetings, workshops, virtual meetings through Webinar and conference calls
- Ability to conduct auditable site visits

Application Checklist

- Is application organized per instructions in the RFA?
- Have the review criteria been addressed in the proposal?
- Are the proposed specific aims achievable in the given time frame?
- Has collaboration been established and partners on board?
- Has the transition plan (for DMCC) been clearly laid out and described for reviewers?
- Has a contact PI been identified for multi-PI proposals and communication and management plan developed?
- Have the special requirements been followed in developing the proposal, e.g., page limit, team structure, study designs, etc.?

Early Detection Research Network



The Early Detection Research Network: Biomarker Developmental Laboratories (BDL) RFA-CA-14-014

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Purpose of this Funding Opportunity Announcement (FOA)

This FOA solicits applications for EDRN Biomarker Developmental Laboratories (BDLs) to discover and develop biomarkers and molecular and cellular signatures for risk assessment, detection, and diagnosis and prognosis of early cancers.

Facilitate the discovery, development, characterization, and testing of new, or the refinement of existing biomarkers and biomarker assays for:

- Risk assessment
- Detection
- Molecular diagnosis and prognosis of early cancer
- Partner with EDRN Clinical Validation Centers (CVCs) and EDRN Reference Laboratories (BRLs)

Examples of Biomarker Discovery Research

- Development of molecular signatures based on **integrated “Omics” approaches** to assess risk; to identify pre-cancerous lesions and early stage cancer; and to identify cancers that are likely to progress.
- Development of biomarkers in preclinical specimens to **discriminate between screen-detected aggressive lesions and indolent or slow-growing lesions**, to reduce the burden of overdiagnosis and overtreatment.
- Development of biomarkers for **risk stratification**; and to **improve pathological classification and stratification**, especially of early lesions.
- Molecular signatures for risk of and early stage disease due to **infectious agents, pathogens**, or environmental agents.

Examples of Biomarker Discovery Research (Continued)

- Development of **integrated approaches** based on **imaging modalities and molecular biomarkers** for risk assessment, early detection, diagnosis and early cancer prognosis.
- Effectively delineate disease **genotypes** and **phenotypes of pre-cancerous and cancerous lesions that are likely to progress.**
- Determine the potential of **perturbed network- and pathway-based biomarkers.**

Phases that BDLs Participate in:

<i>Preclinical Exploratory</i>	PHASE 1	<i>Promising directions identified</i>
<i>Clinical Assay and Validation</i>	PHASE 2	<i>Clinical assay detects established disease</i>
<i>Retrospective Longitudinal</i>	PHASE 3	<i>Biomarker detects preclinical disease and a “screen positive” rule defined</i>
<i>Prospective Screening</i>	PHASE 4	<i>Extent and characteristics of disease detected by the test and the false referral rate are identified</i>
<i>Cancer Control</i>	PHASE 5	<i>Impact of screening on reducing burden of disease on population is quantified</i>

Page Limitations

All page limitations described in the SF424 Application Guide and the Table of Page Limits must be followed, with the following exception:

For this specific FOA, the Research Strategy must not exceed 30 pages.

Requirements and Key Components for a BDL Application

Facilities and Resources

- Specialized or unique resources important for achieving objectives
- PDs/PIs must have their own research laboratories and demonstrate that they have expertise in the technologies they propose to use.

Key Personnel (include or have access to)

- Pathologist - expertise in your disease focus
- Clinical epidemiologist/biostatistician – understands PRoBE study design and the strength (power calculations) of your study design
- A designated Project Manager who will be the main point-of-contact regarding the details and activities of the study

Budget

- Direct costs may not exceed \$250K/yr for single-PD/PI or \$400K/yr for multi-PD/PI applications, including the 30% set-aside.
- The lead PD/PI must commit a minimum of 1.8 person-months effort per year. For multiple PD/PI awards, the other PDs/PIs must devote a minimum of 1.2 person-months effort per year.
- For new applicants, set aside 30% of the annual budget for Network collaborative studies only for years 2-5 . Release of these funds must be reviewed by the EDRN Steering Committee and approved by NCI.
- Travel and per diem expenses for at least one PD/PI and an additional senior investigator to attend:
 - Orientation and Planning Meeting in the first year
 - Two Steering Committee Meetings per year
 - One Network Workshop or Symposium every 18 months

Budget (Continued)

An example of 1st year restricted travel budget for 2 PIs attending 3 Meetings

C. Equipment Description		
List items and dollar amount for each item exceeding \$5,000		
Equipment item		Funds Requested (\$)
<input type="text"/>		<input type="text"/>
Additional Equipment:	<input type="text"/>	<input type="button" value="Add Attachment"/> <input type="button" value="Delete Attachment"/> <input type="button" value="View Attachment"/>
Total funds requested for all equipment listed in the attached file		<input type="text"/>
Total Equipment		<input type="text"/>
D. Travel		Funds Requested (\$)
1. Domestic Travel Costs (Incl. Canada, Mexico and U.S. Possessions)	(2 PIs x 3 Mtgs x \$2,000)	<input type="text" value="12,000"/>
2. Foreign Travel Costs		<input type="text"/>
Total Travel Cost		<input type="text" value="12,000"/>
E. Participant/Trainee Support Costs		Funds Requested (\$)
1. Tuition/Fees/Health Insurance		<input type="text"/>
2. Stipends		<input type="text"/>
3. Travel		<input type="text"/>
4. Subsistence		<input type="text"/>
5. Other	<input type="text"/>	<input type="text"/>
<input type="text"/>	Number of Participants/Trainees	Total Participant/Trainee Support Costs
		<input type="text"/>

F. Other Direct Costs		Funds Requested (\$)
1.	Materials and Supplies	
2.	Publication Costs	
3.	Consultant Services	
4.	ADP/Computer Services	
5.	Subawards/Consortium/Contractual Costs	
6.	Equipment or Facility Rental/User Fees	
7.	Alterations and Renovations	
8.	Network Collaborative Studies (30% of direct costs)	120,000
9.		
10.		
Total Other Direct Costs		120,000

G. Direct Costs	Funds Requested (\$)
Total Direct Costs (A thru F)	400,000

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Total Indirect Costs			<input type="text"/>

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested (\$)
Total Direct and Indirect Institutional Costs (G + H)	<input type="text"/>

J. Fee	Funds Requested (\$)
	<input type="text"/>

K. Budget Justification

(Only attach one file.)

Incumbents must set aside 30% of their budget from the 1st year onward for Network collaborative studies.

- 30% of the \$400K (direct cost) = \$120K (direct cost)

- The remaining budget, \$400K - \$120K = **\$280K** (direct cost) will be used towards the proposed BDL studies.

New applicants must set aside 30% of their budget for Network collaborative studies from 2nd year onward.

Organization of Application and Research Strategy

All standard SF424 instructions for PHS 398 Research Plan must be followed along with the additional items listed below:

- A) Overview** – team structure, relevant partnerships or collaborations, data & resource sharing
- B) Previous Accomplishments** – related to biomarker discovery
 - Incumbent EDRN investigators must include Progress Report with a synopsis of the last site visit report
- C) Research Project** – what you propose to do
 - Rationale, Significance and Objectives
 - Study Design
 - Statistical Considerations
 - Details of samples available

Organization of Application and Research Strategy (Continued)

D) Project Management Plan

1. Timeline
2. Milestones (quantifiable)
3. Decision-tree scheme (when to stop or continue with biomarkers)

Resource Sharing Plan

1. Resource and Specimen Sharing
2. Intellectual Property Management Plan

Receipt and Review Schedule

- Letter of Intent Receipt Date: December 6th, 2014
- Application Receipt Date: January 20, 2015
- Peer Review Date: May 2015
- Advisory Council Review: August, 2015
- Earliest Anticipated Start Date: September 1st 2015

Summary

- Propose biomarker Phase 1/Phase 2 biomarker discovery studies addressing unmet clinical needs
- Highlight key personnel, incorporation of PRoBE design, relevant statistical considerations of study design, and measurable research milestones
- Collaboration with national networks and NCI-supported programs for access to high quality specimens
- Access to specific patient populations for prospective specimen collections
- Partnership with other EDRN components
- Project management plan with timelines and quantitative milestones
- Resource and data sharing plan, and Intellectual Property management plan

NCI PD Contacts

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**Early
Detection
Research
Network**



**Biomarker Reference Laboratories (BRL)
RFA-CA-14-016**

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Purpose and Scope

This Funding Opportunity Announcement (FOA) solicits applications for the EDRN Biomarker Reference Laboratories (BRLs).

BRLs serve as Network resources for the validation of biomarkers for clinical or laboratory use. Their responsibilities include:

- Testing of candidate biomarkers
- Assay design and development
- Assay optimization and refinement
- Assay methods and protocol standardization

Core Responsibilities

(1). Product Development – (Full 5-year plan supported by 70% of the direct costs budget)

***Focus:** develop diagnostic assays for early detection of cancer. The plan must include:*

- clinical significance and intended use of the assay
- description of key technologies, objectives, innovation, and diagnostic services
- performance specifications (especially in comparison to existing assays, methods, and technologies)
- summary of discussions with FDA, if any
- documentation for compliance with GLP and CLIA

Specific Research Objectives and Requirements

BRLs from academic institutions are required to demonstrate substantive participation in the designated project by, at least, one industry partner.

BRLs must have a quality control program and follow Clinical Laboratory Improvement Amendments (CLIA) and the Good Laboratory Practice (GLP) guidelines.

Core Responsibilities (Continued)

(2). Network Collaborative Studies – (30% of the direct costs budget) – these studies may be requested by the EDRN Steering Committee. BRLs will be participating in collaborative studies with BDLs and CVCs.

Focus:

- May include all aspects of assay development and/or reagents and technology development/refinement;
- Protocol/methods standardization, evaluation of accuracy, precision, reproducibility and performance characteristics

Examples of possible projects:

- Analytical validation of published candidate biomarkers, which were not previously validated (e.g., candidate biomarkers discovered through the NCI TCGA project)
- Validation of putative cancer risk makers
- Development and verification of affinity reagents for high throughput quantitative analysis of new biomarkers
- Development of standardized technologies, assays and methods for validation of proteins, peptides, transcripts or metabolites as candidate biomarkers
- Development of innovative assay(s) for detection of cancer from premalignant lesions (e.g., DCIS, HPIN) from exfoliated cells of early cancer patients (e.g., urine sediment of bladder cancer)

Page Limitations

All page limitations described in the SF424 Application Guide and the Table of Page Limits must be followed, with the following exception:

For this specific FOA, the Research Strategy must not exceed 30 pages.

Direct costs may not exceed \$300,000 per year, including the 30% set-aside for Network Collaborative Studies.

- Release of these Network Collaborative Studies funds must be reviewed/recommended by the EDRN Steering Committee and approved by NCI

The PD/PI must commit a minimum of 1.0 person-month effort per year.

Travel and per diem expenses for PD/PI and an additional senior investigator to attend:

- Orientation and Planning Meeting in the first year
- Two Steering Committee Meetings per year
- Scientific Workshop every 18 months

An example of 1st year restricted travel budget for 2 PIs attending 3 Meetings

C. Equipment Description		Funds Requested (\$)
List items and dollar amount for each item exceeding \$5,000		
Equipment item		
<input style="width: 95%;" type="text"/>		<input style="width: 95%;" type="text"/>
Additional Equipment:	<input style="width: 200px;" type="text"/>	<input type="button" value="Add Attachment"/> <input type="button" value="Delete Attachment"/> <input type="button" value="View Attachment"/>
Total funds requested for all equipment listed in the attached file		<input style="width: 100%;" type="text"/>
Total Equipment		<input style="width: 100%;" type="text"/>
D. Travel		Funds Requested (\$)
1. Domestic Travel Costs (Incl. Canada, Mexico and U.S. Possessions)	(2 PIs x 3 Mtgs x \$2,000)	12,000
2. Foreign Travel Costs		<input style="width: 95%;" type="text"/>
Total Travel Cost		12,000
E. Participant/Trainee Support Costs		Funds Requested (\$)
1. Tuition/Fees/Health Insurance		<input style="width: 95%;" type="text"/>
2. Stipends		<input style="width: 95%;" type="text"/>
3. Travel		<input style="width: 95%;" type="text"/>
4. Subsistence		<input style="width: 95%;" type="text"/>
5. Other	<input style="width: 400px;" type="text"/>	<input style="width: 95%;" type="text"/>
<input style="width: 30px;" type="text"/> Number of Participants/Trainees	Total Participant/Trainee Support Costs	<input style="width: 95%;" type="text"/>

F. Other Direct Costs		Funds Requested (\$)
1. Materials and Supplies		
2. Publication Costs		
3. Consultant Services		
4. ADP/Computer Services		
5. Subawards/Consortium/Contractual Costs		
6. Equipment or Facility Rental/User Fees		
7. Alterations and Renovations		
8. Network Collaborative Studies (30% of direct costs)		90,000
9.		
10.		
Total Other Direct Costs		300,000

G. Direct Costs	Funds Requested (\$)
Total Direct Costs (A thru F)	300,000

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Total Indirect Costs			<input type="text"/>

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested (\$)
Total Direct and Indirect Institutional Costs (G + H)	<input type="text"/>

J. Fee	Funds Requested (\$)
	<input type="text"/>

K. Budget Justification
 (Only attach one file.)

Incumbents must set aside 30% from 1st year onward

- 30% of \$300K (direct cost) = **\$90K** (direct cost)
- The remaining budget, \$300K - \$90K = **\$210K** (direct cost) will be used towards the proposed BRL Product Development Studies.

New applicants must set aside 30% from 2nd year onward

- A brief justification must be provided by new applicants as to the changes in Budget and/or Research Plan to accommodate the 30% set-asides from 2nd year onward.

Application Organization and Special Requirements

All standard SF424 instructions for PHS 398 Research Plan must be followed along with the additional items listed below:

- 1. Specific Aims** – focused on the proposed product development and specific unmet need
- 2. Research Strategy** –
 - **Sub-section A: Overview**
 - **Sub-section B: Previous Accomplishments** - (Progress reports included for renewals, only)
 - **Sub-section C: Plans for the Required Areas of Responsibility** - (include milestones and timeline)
- 3. Network Collaborative Studies**
- 4. Industry Participation**
- 5. Resource and Data Sharing and IP Management Plan**

Applicants for BRL funding should address the following:

- Quality Improvement plans with CLIA and/or CAP and GLP certification
- Define previous expertise in analytic validation of biomarker assays
- Delineate a complete product development plan for biomarker validation
- Demonstrate partnership with Industry

Contact Information

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Jo Ann Rinaudo, Ph.D.
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**Early
Detection
Research
Network**



**Clinical Validation Centers
RFA-CA-14-015**

Christos Patriotis, Ph.D.

patriotisc@mail.nih.gov

**Sharmistha Ghosh-Janjigian,
Ph.D.**

ghoshjanjigias@mail.nih.gov



Purpose of this Funding Opportunity Announcement (FOA)

This FOA solicits applications for EDRN Clinical Validation Centers (CVCs), responsible for conducting clinical research on the validation of biomarkers and serving as clinical resource centers for the EDRN.

Scope

- Conduct Biomarker Validation Studies
- Partner with other networks with available biospecimens for biomarker validation (e.g., NCORP, NCTN, Cohort Consortium, HMOs)
- Serve as a Collaborative Resource for the Network
- Partner with EDRN Biomarker Developmental Laboratories (BDLs) and EDRN Reference Laboratories (BRLs)

Biomarker Validation Studies

- Conduct clinical research on the validation of biomarkers for risk assessment, detection, diagnosis and prognosis of early cancer. This research must conform to EDRN-defined Phase 2 or Phase 3 biomarker studies.
- The proposed research must be presented in your U01 application and will be evaluated by the review panel convened by NCI's Division of Extramural Activities.
- Non-Responsive to FOA: Biomarker discovery projects are not appropriate for this RFA

Phase 2 and Phase 3 Studies

- Phase 2 studies are to determine the capacity of biomarkers to distinguish people with cancer from those without or determine the accuracy of biomarkers to predict progression from a precancerous lesion to cancer
- Phase 3 studies are to assess the capacity of a biomarker to detect preclinical disease by testing the marker against specimens collected longitudinally by research cohorts
- There must be supporting data (e.g. sensitivity and specificity) on the proposed biomarkers from either the applicant or others

An Example of a Phase 2/Phase 3 Biomarker Validation Study

EDRN-SPORE-PLCO Phase 2/Phase 3 Study for Validation of a Biomarker Consensus Panel for Early Detection of Ovarian Cancer

- Phase 2: 70 biomarkers tested on a blinded set of sera from 80 early stage and 80 late stage ovarian cancer cases collected at diagnosis, 160 controls with benign disease, and 480 healthy controls.
 - Goal: Rank candidates based on Sensitivity determined at 95% and 98% Specificity.
- Phase 3: 32 top performing markers from Phase 2 were tested on 118 cases of proximate specimens from PLCO collected within 6 months and up to 7 years prior to diagnosis of ovarian cancer versus 476 matched healthy controls.
 - Goal: Determine Sensitivity and PPV at 95% and 98% Specificity.

Partner with Other Networks and Organizations

Broaden coverage of different organ sites and patient accrual through formal collaborations with:

- Networks (NCTN, NCORP, etc.)
- Cohort Consortium
- Health Maintenance Organizations
- Other NCI supported Programs and infrastructures (SPOREs, PLCO, Breast and Colon Cancer Family Registries, etc.)
- Other Federal Agencies

Collaborative Resource for EDRN

- **Serve as a resource center for collaborative research within the Network by:**
 - participating in collaborative biomarker validation studies under the coordination of the EDRN Steering Committee
 - contributing biospecimens and developing guidelines for the formation of EDRN reference sets
 - providing high quality biological specimens to other EDRN investigators for use in biomarker discovery
 - types and quantities of specimens will be agreed upon post-award between the individual CVC and BDL and NCI
- **Lead discussions with the relevant EDRN Collaborative Group on the inclusion of biomarkers in the EDRN Biomarker Database**

Prospective Specimen Collections

- **Specimens can be collected prospectively only to support:**
 - validation studies proposed in the application
 - EDRN Reference Set collections
 - requests from other EDRN investigators that have been recommended by the Steering Committee and approved by NCI
 - collaborations with ongoing trials that provide a unique opportunity for prospective longitudinal collection of specimens for major epithelial cancers or cancers with high morbidity and mortality
- All specimens must be collected using a well-designed SOP such as PRoBE or a similar study design.
- **Restricted set-aside funds may be used to support specimen collections for reference sets and to support requests from other investigators**

Partner with EDRN BDLs and BRLs

- **After awards are made, NCI will work with CVCs and BDLs to establish partnerships. CVCs will:**
 - consult with BDLs on clinical issues such as selection of subjects and specimens and biomarker performance parameters
 - provide the BDLs with adequate specimens for biomarker discovery and development
- **CVCs will work with BDLs to validate biomarkers developed in their laboratories**
- **Where appropriate, a CVC will partner with an EDRN BRL that has the expertise to develop clinical-grade assays for biomarker validation**

Page Limitations

All page limitations described in the SF424 Application Guide and the Table of Page Limits must be followed, with the following exception:

For this specific FOA, the Research Strategy must not exceed 30 pages.

Budget

- **Direct costs may not exceed \$600,000 per year, including the 30% set-aside**
- **The lead PD/PI must commit a minimum of 1.8 person-months effort per year. For multiple PD/PI awards, the other PDs/PIs must devote a minimum of 1.2 person-months effort per year**
- **Travel and per diem expenses for at least a PD/PI and an additional senior investigator to attend:**
 - Orientation and Planning Meeting in the first year
 - Two Steering Committee Meetings per year
 - Network Workshop or Symposium every 18 months
- **30% of the annual budget must be set-aside for Network collaborative studies or collecting specimens to fulfill specific Network needs. Release of these funds must be reviewed/recommended by the EDRN Steering Committee and approved by NCI**

An example of 1st year restricted travel budget for 2 PIs attending 3 Meetings

C. Equipment Description		
List items and dollar amount for each item exceeding \$5,000		
Equipment item	<input type="text"/>	Funds Requested (\$) <input type="text"/>
Additional Equipment:	<input type="text"/>	<input type="button" value="Add Attachment"/> <input type="button" value="Delete Attachment"/> <input type="button" value="View Attachment"/>
Total funds requested for all equipment listed in the attached file		<input type="text"/>
Total Equipment		<input type="text"/>
D. Travel		Funds Requested (\$)
1. Domestic Travel Costs (Incl. Canada, Mexico and U.S. Possessions)(2 PIs x 3 Mtgs x \$2,000)		<input type="text" value="12,000"/>
2. Foreign Travel Costs		<input type="text"/>
Total Travel Cost		<input type="text" value="12,000"/>
E. Participant/Trainee Support Costs		Funds Requested (\$)
1. Tuition/Fees/Health Insurance		<input type="text"/>
2. Stipends		<input type="text"/>
3. Travel		<input type="text"/>
4. Subsistence		<input type="text"/>
5. Other	<input type="text"/>	<input type="text"/>
<input type="text"/> Number of Participants/Trainees	Total Participant/Trainee Support Costs	<input type="text"/>

F. Other Direct Costs		Funds Requested (\$)
1. Materials and Supplies		
2. Publication Costs		
3. Consultant Services		
4. ADP/Computer Services		
5. Subawards/Consortium/Contractual Costs		
6. Equipment or Facility Rental/User Fees		
7. Alterations and Renovations		
8. Network Collaborative Studies (30% of direct costs)		180,000
9.		
10.		
Total Other Direct Costs		600,000

G. Direct Costs	Funds Requested (\$)
Total Direct Costs (A thru F)	600,000

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)
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Total Indirect Costs			<input type="text"/>

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested (\$)
Total Direct and Indirect Institutional Costs (G + H)	<input type="text"/>

J. Fee	Funds Requested (\$)
	<input type="text"/>

K. Budget Justification

(Only attach one file.)

Incumbents must set aside 30% from 1st year onward

New applicants must set aside 30% from 2nd year onward

- A brief justification must be provided by new applicants as to the changes in Budget and/or Research Plan to accommodate the 30% set-asides from 2nd year onward.

Special Requirements: Research Plan

All standard SF424 instructions for PHS 398 Research Plan must be followed along with the additional items listed below:

Relevant recent accomplishments - All applications

Progress Report - Renewal applications only

- Biomarker research and specimen collections in previous application & projects supported by set-aside funds and the EDRN Core Fund
- Participation in EDRN activities and collaborations
- Synopsis of latest Programmatic site visit

Organization of the CVC

- Team structure, expertise and available resources, including access to high quality biospecimen collections
- Leadership Plan (for multi-PD/PI applications)

Special Requirements (Continued)

- **Research Project**
 - Biomarker Validation Studies
 - Capabilities for prospective patient accrual
- **Collaborative Resource for the Network**
 - Collaborative activities
 - Partnering with EDRN BDLs and BRLs
 - Specimen collection guidelines
 - Biomarker database – Expert review of biomarker related data/information
- **Project Management Plan**
 - Timelines & quantitative milestones – after 3 years, progress will be evaluated by NCI during a site visit

Summary

- Clinical and epidemiological expertise
- Collaboration with national networks and NCI-supported programs for access to high quality specimens
- Access to specific patient populations for prospective specimen collections
- Quality Assurance and Quality Control procedures
- Phase 2/Phase 3 biomarker validation studies addressing unmet clinical needs
- Partnership with other EDRN components
- Project management plan with timelines and quantitative milestones
- Resource and data sharing plan, and Intellectual Property management plan

Contact Information

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Sharmistha Ghosh-Janjigian, Ph.D.
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**Early
Detection
Research
Network**



**Data Management and Coordinating Center
RFA-CA-14-017**

Nadarajen A. Vydelingum, Ph.D.

vydelinn@mail.nih.gov

Paul Wagner, Ph.D.

wagnerp@mail.nih.gov



Purpose of this Funding Opportunity Announcement (FOA)

This FOA solicits applications for the EDRN Data Management and Coordinating Center (DMCC) from investigators with expertise in data management, protocol development, biostatistics, and information technology, and in coordinating and providing logistical support for meetings and conferences.

Part 1. Section 1 Specific Responsibilities and Requirements

Scope: Responsibilities

1. Network Coordination
2. Data Management and Protocol Development
3. Validation Infrastructure and Services
4. EDRN Core Fund Management

1. Network Coordination

- Provide logistical and administrative support for EDRN meetings, workshops, and conference calls.
- Produce and maintain documents, including Manual of Operations, and maintain the EDRN central filing system.
- Enhance and maintain EDRN interactive and secure websites.
- Enhance and maintain an interactive mail system for communication within the Network.

Enhance and Maintain Public Portal

Home

About EDRN

Biomarkers

Protocols

Science Data

Publications

Resources

Specimens



Collaborative
Groups



Secure Site



Public, Patients,
Advocates



Funding
Opportunities



Sites



Member Directory



Committees



Biomarker
Informatics
Standards



Division of Cancer
Prevention



Cancer Biomarkers
Research Group



Bookshelf

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Welcome to EDRN

The Early Detection Research Network (EDRN), an initiative of the National Cancer Institute (NCI), brings together dozens of institutions to help accelerate the translation of biomarker information into clinical applications and to evaluate new ways of testing cancer in its earliest stages and for cancer risk.



Research and development of biomarkers and technologies for the clinical application of early cancer detection strategies

Getting Started...

Check out the [EDRN Highlights](#) — a listing of our accomplishments and milestones.

► [Scientific Components](#)

► [For Public, Patients, Advocates](#)

► [Collaborative Opportunities](#) (how to join EDRN)

► [For Researchers](#)

Search Site

 Search

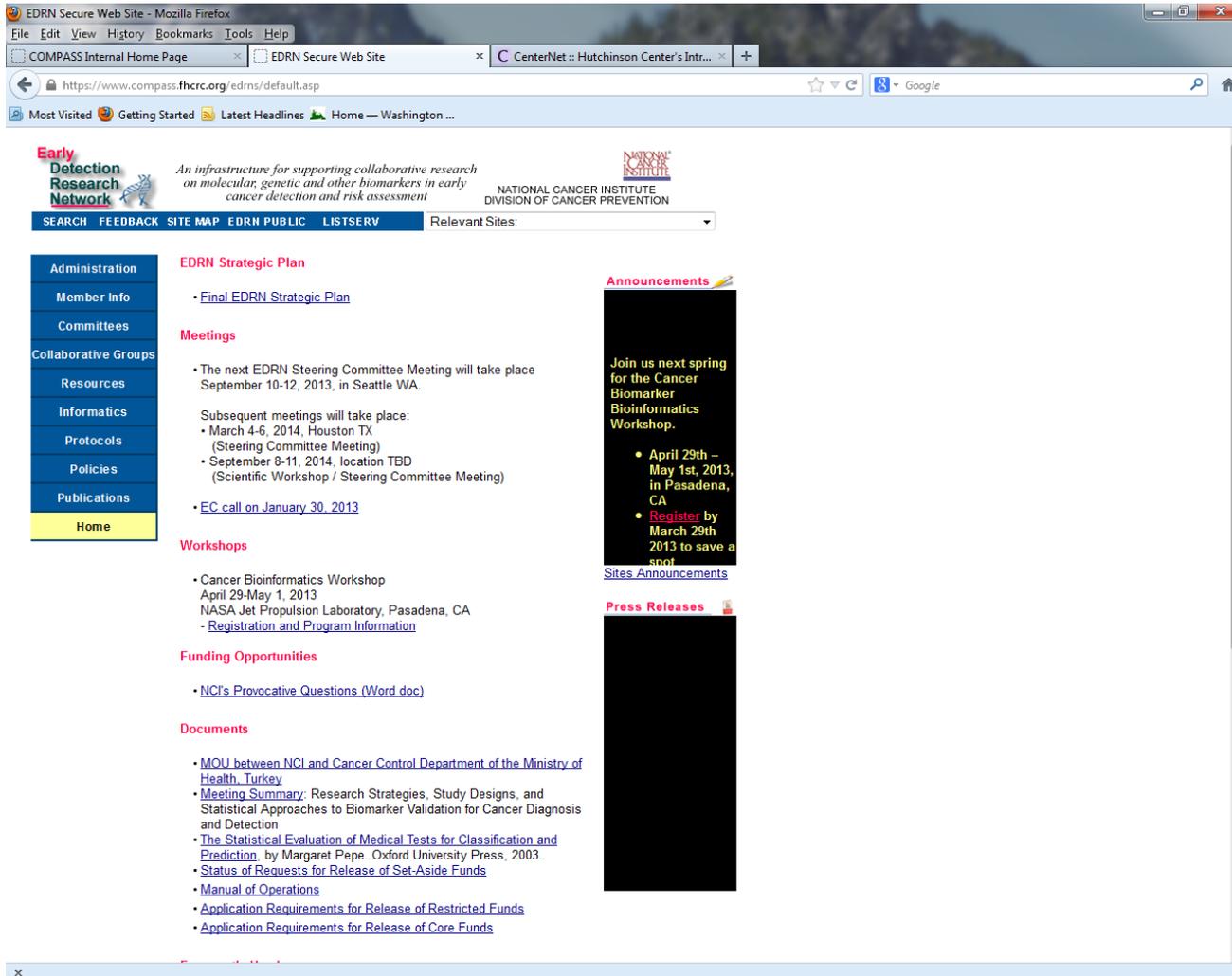
Cancer Biomarker Bioinformatics Workshop

Join us for the Cancer Biomarker Bioinformatics Workshop.

- April 29th–May 1st 2013 in Pasadena, CA
- Register to save a spot
- Registration is **free**
- Full program and other details available

[Announcement](#)

Enhance and Maintain Secure Website



EDNR Secure Web Site - Mozilla Firefox

File Edit View History Bookmarks Tools Help

COMPASS Internal Home Page | EDNR Secure Web Site | CenterNet :: Hutchinson Center's Intr...

https://www.compass.fhcr.org/ednrs/default.asp

Most Visited Getting Started Latest Headlines Home — Washington ...

Early Detection Research Network  *An infrastructure for supporting collaborative research on molecular, genetic and other biomarkers in early cancer detection and risk assessment*

NATIONAL CANCER INSTITUTE
DIVISION OF CANCER PREVENTION

SEARCH FEEDBACK SITE MAP EDNR PUBLIC LISTSERV Relevant Sites: [dropdown]

Administration

- Member Info
- Committees
- Collaborative Groups
- Resources
- Informatics
- Protocols
- Policies
- Publications
- Home**

EDNR Strategic Plan

- [Final EDNR Strategic Plan](#)

Meetings

- The next EDNR Steering Committee Meeting will take place September 10-12, 2013, in Seattle WA.
- Subsequent meetings will take place:
 - March 4-6, 2014, Houston TX (Steering Committee Meeting)
 - September 8-11, 2014, location TBD (Scientific Workshop / Steering Committee Meeting)
- [EC call on January 30, 2013](#)

Workshops

- Cancer Bioinformatics Workshop
April 29-May 1, 2013
NASA Jet Propulsion Laboratory, Pasadena, CA
[Registration and Program Information](#)

Funding Opportunities

- [NCI's Provocative Questions \(Word doc\)](#)

Documents

- [MOU between NCI and Cancer Control Department of the Ministry of Health, Turkey](#)
- [Meeting Summary: Research Strategies, Study Designs, and Statistical Approaches to Biomarker Validation for Cancer Diagnosis and Detection](#)
- [The Statistical Evaluation of Medical Tests for Classification and Prediction](#), by Margaret Pepe, Oxford University Press, 2003.
- [Status of Requests for Release of Set-Aside Funds](#)
- [Manual of Operations](#)
- [Application Requirements for Release of Restricted Funds](#)
- [Application Requirements for Release of Core Funds](#)

Announcements

Join us next spring for the Cancer Biomarker Bioinformatics Workshop.

- April 29th – May 1st, 2013, in Pasadena, CA
- [Register by March 29th 2013 to save a spot!](#)

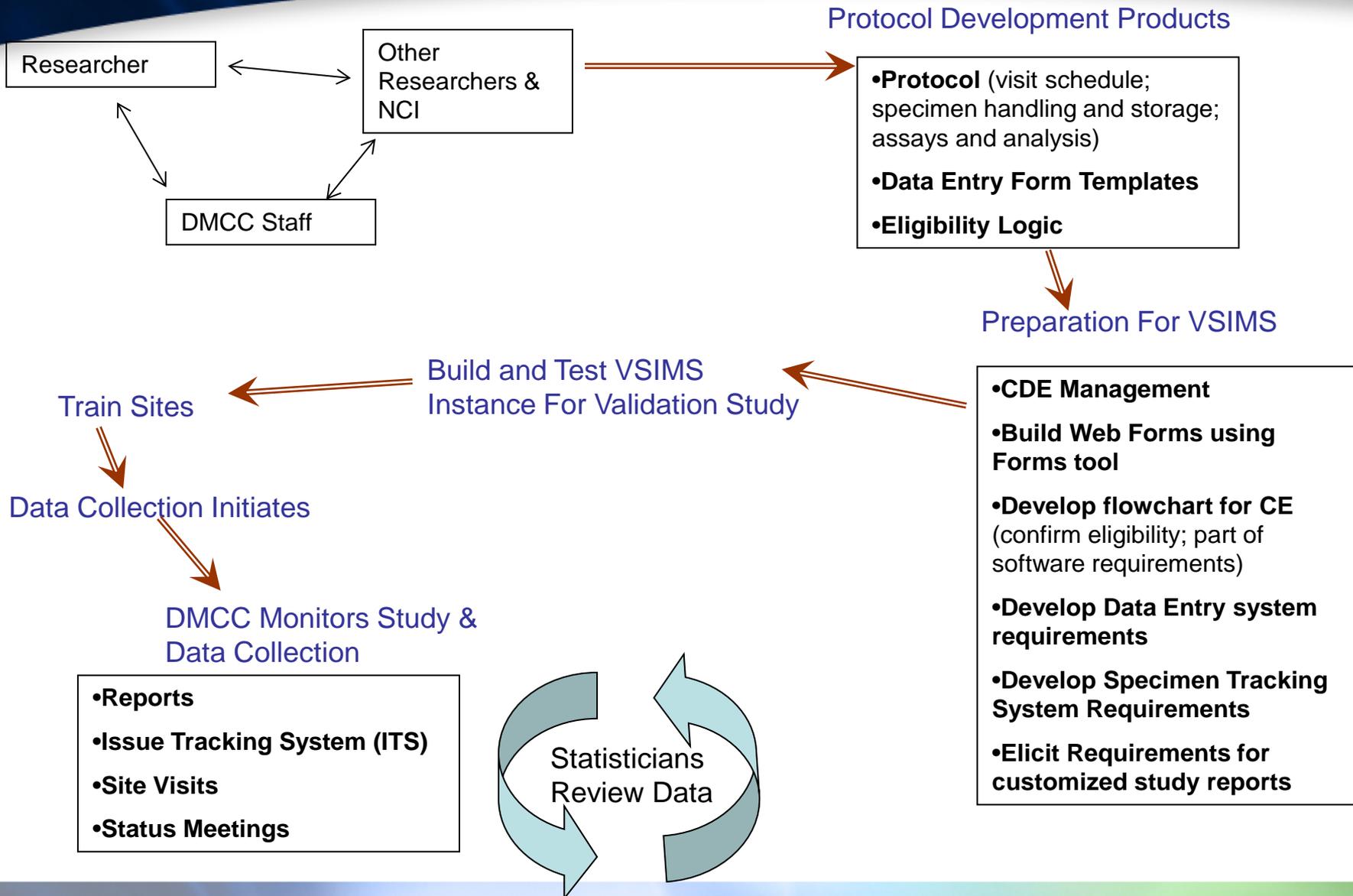
[Sites Announcements](#)

Press Releases

2. Data Management and Protocol Development

- **Provide coordination and support for EDRN collaborative validation studies and other collaborative projects approved by the EDRN Steering Committee:**
 - Work with investigators on study design and protocol development
 - Provide statistical analysis
 - Produce data forms and protocol manuals
 - Develop and maintain a data management system
 - Monitor protocol adherence, data collection and data submission
 - Analyze data, provide reports and assist in writing manuscripts
- **Support the formation and distribution of EDRN biospecimen reference sets and analyze data that result from the use of these specimens.**
- **Develop uniform investigative protocols for data and specimen collection.**

Protocol Development



3. Validation Infrastructure and Services

Enhance and maintain informatics and infrastructure services for biomarker development

- Validation Study Information Management System (VSIMS)

Partner with EDRN Informatics Center at NASA's Jet Propulsion Laboratory to maintain and enhance information technology infrastructure for

- EDRN Resource Network Exchange
- EDRN Knowledge Environment
- EDRN Catalog and Archive Service
- EDRN Study Information System
- EDRN Biomarker Database

Validation Study Information Management System (VSIMS)

- Assemblage of tools that collects study data and assists with management of EDRN validation studies
- Data collection tools (Data entry system, specimen tracking system, eligibility checks)
- Study monitoring tools (Reports: Enrollment, master lists, data collection monitoring)
- Communication tools (Issue tracking system, data transfer, statisticians page)
- Administration tools (directories, MOO, SOP, ID generators)
- NCI anticipates that in the future in any given year the DMCC will coordinate approximately six Network trials involving on average 10 study sites and biospecimen reference set collections.

Examples of VSIMS Study Support

Monitor data quality and provide ongoing support:

- Site visits
- Issue tracking system
- Help line
- Study announcements
- DQMB or DSMC
- Manuals of Operation
- Protocol revisions

	Completed for:
	SELDI
	Lung/CARET
	Barrett's Esophagus
	EDRN/WHI Colon
	Mesothelioma
	Ovarian/Yale
	Ovarian/PLCO
	proPSA
	Canary Never Smokers
	Canary TMA
	Breast Ref
✓	DCP & Liver Ref
	Lung Ref
	Pancreatic Ref
	Prostate Ref
	Colon Ref
	Cancer in Women Ref
✓	MSA & Bladder Ref
✓	PCA3 & Prostate Ref
	Triple Negative Breast
✓	Canary PASS
	Benign Breast Disease (BBD)
	DCIS
✓	Pancreatic Cyst Ref
✓	GLNE 010 Colon
✓	Lung Nodule
✓	HEDS



An infrastructure for supporting
validation studies in the EDRN
Sponsored by National Cancer Institute



Protocol: MSA (ID: 108) User: Qing Xiao (Site ID: 128)

[Logout](#) [Home](#) [Back](#) [Print](#) [VSIMS](#)

Staff Name: Qing Xiao
MSA Role: None

▣ **Early Detection Research Network Validation Study** (Baseline Entry)

- MSA Consent-1.0
- MSA Eligibility-1.0 [Ineligible List \(14 \)](#)
- MSA Baseline-1.21
- MSA Specimen Collection-1.0
- MSA Cystoscopy Procedure and Results (G2 & G3 only)-1.0
- MSA TURBT Procedure and Results (G3 only)-1.0
- MSA Other Procedure and Results (G3 only)-1.0
- MSA Upper Tract Imaging (G3 only)-1.0
- MSA Urinalysis and/or Heme Results (G1 & G2 only)-1.2
- MSA Culture and Sensitivity (CNS) Results (G2 Only)-1.0
- MSA Urine Cytology Results-1.0

Submit

Reset

Confirm Eligibility

Follow-up Form

Main

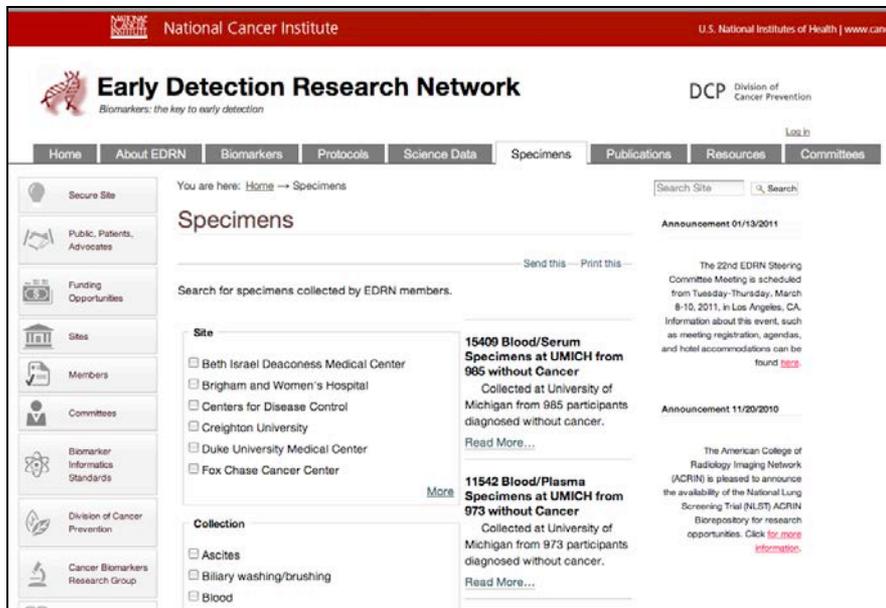
EDRN Resource Network Exchange

- EDRN Resource Network Exchange (ERNE) is used to query data across EDRN's Clinical Validation Centers (CVC)
- The system is based on NASA JPL's Object-oriented Data module which can be easily tailored to the CVC's institutional informatics system.
- ERNE allows the user to query the availability of specimens in real-time.

Distributed Specimen Locator System (ERNE) Query Screen

EDRN Resource Network Exchange (ERNE)

- An *infrastructure* for sharing data resources across EDRN
- Supports *real time* (on demand) *distribution* of data to users
- EDRN CDE Mapping Tool



National Cancer Institute U.S. National Institutes of Health | www.nci.nih.gov

Early Detection Research Network DCP Division of Cancer Prevention
Biomarkers: the key to early detection

Home About EDRN Biomarkers Protocols Science Data **Specimens** Publications Resources Committees

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Search Site Search

Specimens

Search for specimens collected by EDRN members.

Site

- Beth Israel Deaconess Medical Center
- Brigham and Women's Hospital
- Centers for Disease Control
- Creighton University
- Duke University Medical Center
- Fox Chase Cancer Center

Collection

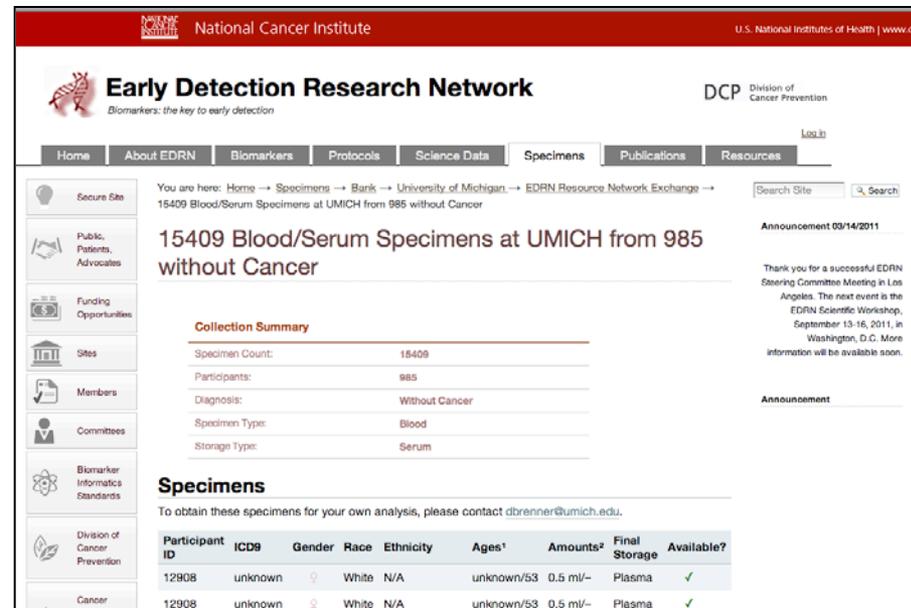
- Ascites
- Biliary washing/brushing
- Blood

15409 Blood/Serum Specimens at UMICH from 985 without Cancer
Collected at University of Michigan from 985 participants diagnosed without cancer.
[Read More...](#)

11542 Blood/Plasma Specimens at UMICH from 973 without Cancer
Collected at University of Michigan from 973 participants diagnosed without cancer.
[Read More...](#)

Announcement 01/13/2011
The 22nd EDRN Steering Committee Meeting is scheduled from Tuesday-Thursday, March 8-10, 2011, in Los Angeles, CA. Information about this event, such as meeting registration, agendas, and hotel accommodations can be found [here](#).

Announcement 11/20/2010
The American College of Radiology Imaging Network (ACRIN) is pleased to announce the availability of the National Lung Screening Trial (NLST) ACRIN Biorepository for research opportunities. Click [for more information](#).



National Cancer Institute U.S. National Institutes of Health | www.nci.nih.gov

Early Detection Research Network DCP Division of Cancer Prevention
Biomarkers: the key to early detection

Home About EDRN Biomarkers Protocols Science Data **Specimens** Publications Resources Committees

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Search Site Search

15409 Blood/Serum Specimens at UMICH from 985 without Cancer

Announcement 03/14/2011
Thank you for a successful EDRN Steering Committee Meeting in Los Angeles. The next event is the EDRN Scientific Workshop, September 13-16, 2011, in Washington, D.C. More information will be available soon.

Announcement

Collection Summary

Specimen Count:	15409
Participants:	985
Diagnosis:	Without Cancer
Specimen Type:	Blood
Storage Type:	Serum

Specimens

To obtain these specimens for your own analysis, please contact dbrenner@umich.edu.

Participant ID	ICD9	Gender	Race	Ethnicity	Ages ¹	Amounts ²	Final Storage	Available?
12908	unknown	♀	White	N/A	unknown/53	0.5 ml/-	Plasma	✓
12908	unknown	♀	White	N/A	unknown/53	0.5 ml/-	Plasma	✓

Maintain and Enhance EDRN Catalog and Archive Service

EDRN eCAS Web Portal

http://edrn.jpl.nasa.gov/ecas/dataset.php?typeID=urn:edrn:FHCRCHanashAnnexinLamr

National Cancer Institute U.S. National Institutes of Health | www.cancer.gov

Early Detection Research Network

DCP Division of Cancer Prevention

Research and development of biomarkers and technologies for the clinical application of early cancer detection strategies Not logged in. [Log in](#)

[Home](#) / Protocol Dataset: FHCRCHanashAnnexinLamr **EDRN CATALOG & ARCHIVE SERVICE**

Autoantibody Biomarkers

Dataset Metadata: [less information \[-\]](#)

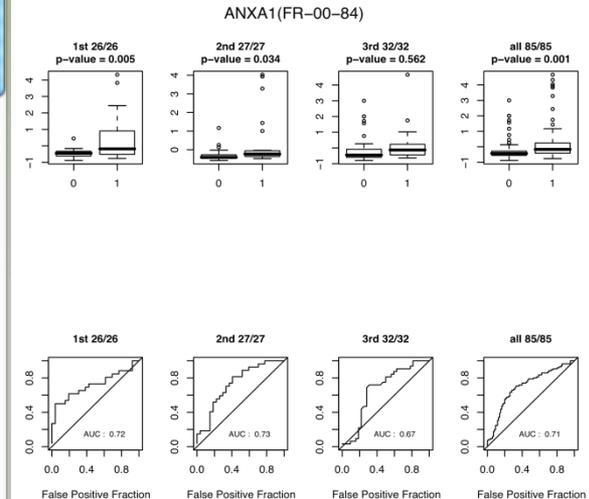
Protocol Name	Validation of Protein Markers for Lung Cancer Using CARET Sera and Proteomics Techniques
Protocol ID	138
Dataset Abstract	We have implemented a high throughput platform for quantitative analysis of serum autoantibodies, which we have applied to lung cancer for discovery of novel antigens and for validation in prediagnostic sera of autoantibodies to antigens previously defined based on analysis of sera collected at the time of diagnosis. RESULTS: We present evidence for the occurrence in lung cancer sera of autoantibodies to annexin I, 14-3-3 theta, and a novel lung cancer antigen, LAMR1, which precede onset of symptoms and diagnosis.
Dataset Name	Autoantibody Biomarkers
Principal Investigator	Samir Hanash
Site Name	Fred Hutchinson Cancer Research Center (Biomarker Developmental Laboratories)
Data Custodian	Ji Qiu
Data Custodian Email	jqiu@fhcrc.org
Organ Site	Lung
Organ Collaborative Groups	Lung and Upper Aerodigestive
Method	Proteins from human lung adenocarcinoma cell line A549 lysates were

1-7 of 7 Products Associated With This Dataset:

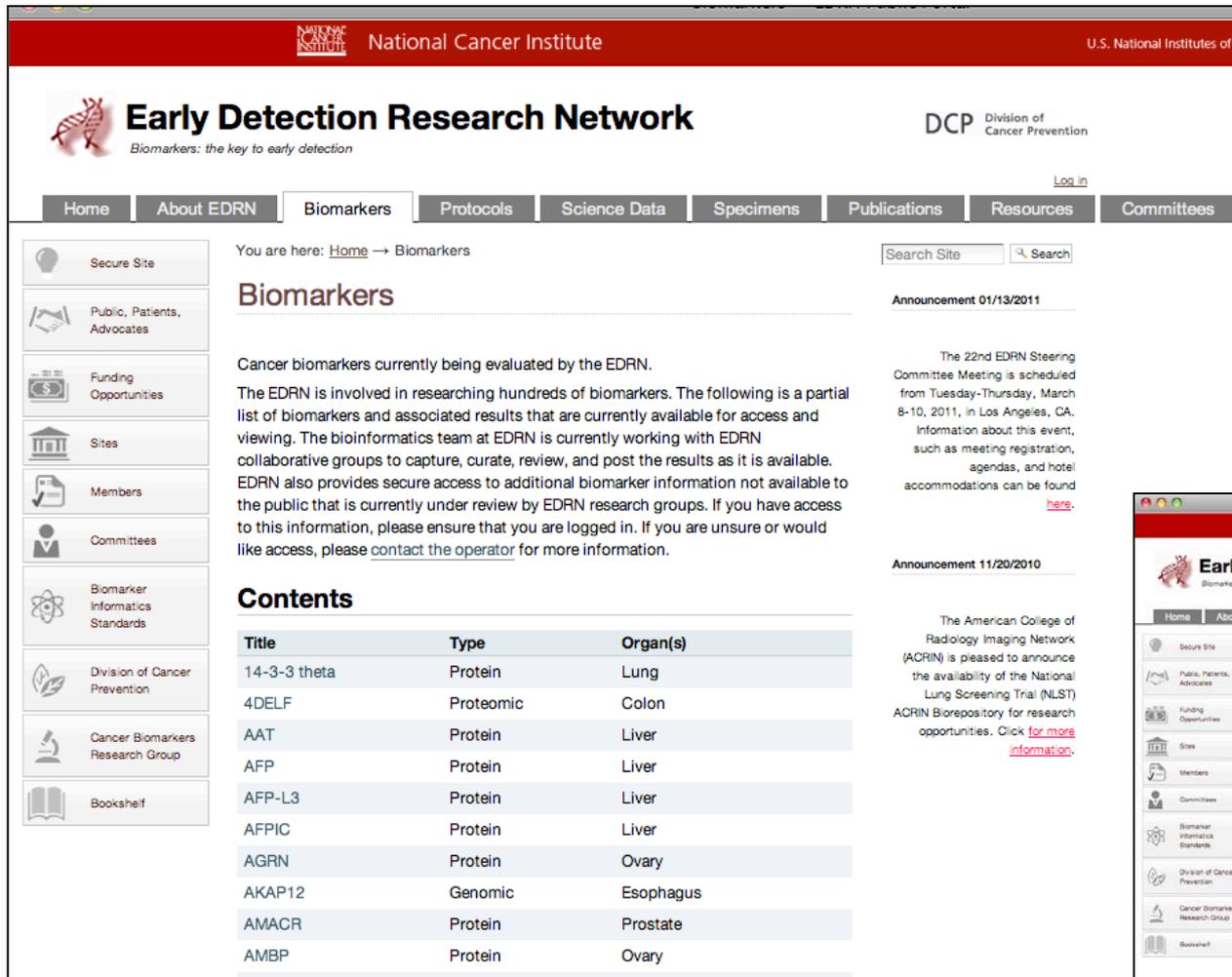
- [\(By Batch\)ANXA1\(FR-00-84\).pdf](#)
- [\(By Batch\)14-3-3.pdf](#)
- [CARET lung cancer.xls](#)
- [\(By Batch\)DI-1.pdf](#)
- [\(By Batch\)LAMR1.pdf](#)
- [\(By Batch\)PGP9.5.pdf](#)
- [annexin+lamr1+14-3-3.pdf](#)

Result Page **1**

Download results



Maintain and Enhance Biomarker Database



National Cancer Institute U.S. National Institutes of Health

Early Detection Research Network
Biomarkers: the key to early detection

DCP Division of Cancer Prevention

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You are here: [Home](#) → Biomarkers

Biomarkers

Cancer biomarkers currently being evaluated by the EDNRN.

The EDNRN is involved in researching hundreds of biomarkers. The following is a partial list of biomarkers and associated results that are currently available for access and viewing. The bioinformatics team at EDNRN is currently working with EDNRN collaborative groups to capture, curate, review, and post the results as it is available. EDNRN also provides secure access to additional biomarker information not available to the public that is currently under review by EDNRN research groups. If you have access to this information, please ensure that you are logged in. If you are unsure or would like access, please [contact the operator](#) for more information.

Contents

Title	Type	Organ(s)
14-3-3 theta	Protein	Lung
4DELf	Proteomic	Colon
AAT	Protein	Liver
AFP	Protein	Liver
AFP-L3	Protein	Liver
AFPIC	Protein	Liver
AGRIN	Protein	Ovary
AKAP12	Genomic	Esophagus
AMACR	Protein	Prostate
AMBp	Protein	Ovary

Search Site Search

Announcement 01/13/2011

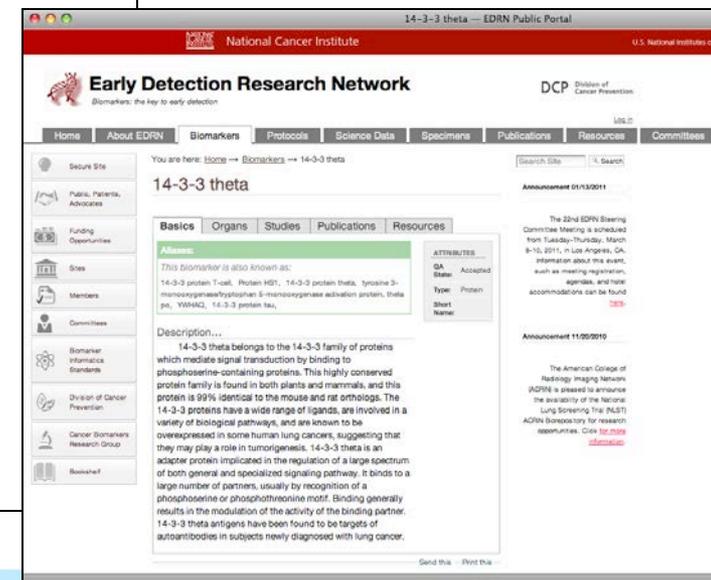
The 22nd EDNRN Steering Committee Meeting is scheduled from Tuesday-Thursday, March 8-10, 2011, in Los Angeles, CA. Information about this event, such as meeting registration, agendas, and hotel accommodations can be found [here](#).

Announcement 11/20/2010

The American College of Radiology Imaging Network (ACRIN) is pleased to announce the availability of the National Lung Screening Trial (NLST) ACRIN Biorepository for research opportunities. Click [for more information](#).

To Capture and Share Biomarker Annotations Provides connection to the following:

- Protocol
- Scientific Data
- Publications
- Additional Biomarker Resources



National Cancer Institute U.S. National Institutes of Health

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Home About EDNRN Biomarkers Protocols Science Data Specimens Publications Resources Committees

You are here: [Home](#) → Biomarkers → 14-3-3 theta

14-3-3 theta

Basics Organs Studies Publications Resources

Aliases:
This biomarker is also known as:
14-3-3 protein 1- α , Protein HD1, 14-3-3 protein theta, tyrosine 3-monoxygenase/tyrosine 5-monoxygenase activation protein, theta iso, YWHAQ, 14-3-3 protein tau.

DESCRIPTION:
14-3-3 theta belongs to the 14-3-3 family of proteins which mediate signal transduction by binding to phosphoserine-containing proteins. This highly conserved protein family is found in both plants and mammals, and this protein is 99% identical to the mouse and rat orthologs. The 14-3-3 proteins have a wide range of ligands, are involved in a variety of biological pathways, and are known to be overexpressed in some human lung cancers, suggesting that they may play a role in tumorigenesis. 14-3-3 theta is an adapter protein implicated in the regulation of a large spectrum of both general and specialized signaling pathway. It binds to a large number of partners, usually by recognition of a phosphoserine or phosphothreonine motif. Binding generally results in the modulation of the activity of the binding partner. 14-3-3 theta antigens have been found to be targets of autoantibodies in subjects newly diagnosed with lung cancer.

ATTRIBUTES:
GA: Basic
Site: Accepted
Type: Protein
Short Name: [View](#)

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Organization of the Application

All instructions in the SF424 (R&R) Application Guide must be followed, with the following additional instructions:

Sub-section A: Overview - advantages of the proposed DMCC to serve as a scientific and organizational hub to the entire Network and explain the anticipated significance and innovation of the proposed strategies for early cancer detection, risk assessment, diagnosis, and prognosis.

Sub-section B: Previous Accomplishments - describe previous research accomplishments/preliminary studies relevant to biomarker development and the goals of the proposed DMCC.

Organization of the Application (Continued)

Sub-section C: Plans for the Required Areas of Responsibility

- Network Coordination
- Data Management and Protocol Development (conducted under the direction of the Steering Committee)
- Validation Information System and Services
- Management of Core Fund

Transition Plan

The incumbent DMCC institution must provide a detailed transition plan and the cost involved in transferring data, software for information technology infrastructures, databases, analytical tools, and other relevant documents resulting from EDRN activities.

Page Limitations

All page limitations described in the SF424 Application Guide and the Table of Page Limits must be followed, with the following exception:

For this specific FOA, the Research Strategy must not exceed 30 pages.

Budget

- **Direct costs may not exceed \$4.5 million per year.**
 - Up to \$ 2.0 million to support DMCC activities
 - \$2.5 million for restricted Network Core Fund
- **30% of the DMCC's annual budget (up to \$600,000 per year direct costs) must be set-aside for Network validation trials and reference set collection. Release of these funds must be reviewed by the EDRN Steering Committee and authorized by NCI.**
- **Travel and per diem expenses for a least the PI and an additional senior investigator to attend:**
 - Orientation and Planning Meeting in the first year
 - Two Steering Committee Meetings per year
 - Network Workshop or Symposium every 18 months (coincides with a Steering Committee Meeting)

Budget (Continued)– Network Core Fund

- \$2.5 million per year must be allocated to the restricted Network Core Fund, which will be used to support post-award Network-wide collaborative studies through sub-contractual arrangements.
- This amount should be presented in the Other Direct Costs category under the heading “Network Core Fund”.
- The exact dollar amount for Core Fund will be determined by the NCI at the time of award.
- Release of these funds must be reviewed by the EDRN Steering Committee and authorized by NCI.

Management of Core Fund

- The DMCC will administer the EDRN restricted Core fund.
- The use of these funds will be restricted to support Network-wide collaborative studies and other resource-related activities, including patient accrual and collection of specimens.
- For activities reviewed and recommended by the EDRN Steering Committee and authorized by NCI, the DMCC will activate funds from the Core Fund by establishing appropriate sub-contractual arrangements with the institutions of the investigators involved.

Other Project Information

Key personnel:

- Describe the knowledge and experience of the PD(s)/PI(s) and other senior/key persons in cancer research and technologies for cancer detection.
- Provide supplemental data documenting your recent research contributions relevant to biomarker validation studies.

Facilities:

- Describe the infrastructure available to the applicants for data storage, data security and data analysis appropriate to support the activities proposed.

Summary

- Provide rigorous study design and development of study protocols.
- Describe your experience in management of large-scale collaborative research.
- Describe the organization of the proposed DMCC and the team's strengths in the various key components.
- Explain how the team will integrate and capitalize on the expertise of its members.

Contact Information

Nadarajen A. Vydelingum, Ph.D.
vydelinn@mail.nih.gov

Paul Wagner, Ph.D.
wagnerp@mail.nih.gov

Early Detection Research Network



Investigator Responsibilities

Jo Ann Rinaudo, Ph.D.

rinaudoj@mail.nih.gov



PI/PD: Individual Responsibilities

Define scientific objectives and approaches including:

- Study design & protocol development
- Data collection & accrual of patients (safety monitoring)
- Data analysis
- Quality control & quality assurance
- Registration of protocol with DMCC
- Publications & presentations – acknowledge EDRN support

PD/PI: Collaborative Responsibilities

- Develop collaborations (Team Building: BDL-BRL-CVC)
- Participate in Network collaborative studies (set-aside projects, validation studies)
- Collaborate with DMCC on common research designs and protocol development (apply EDRN CDEs)
- Data sharing

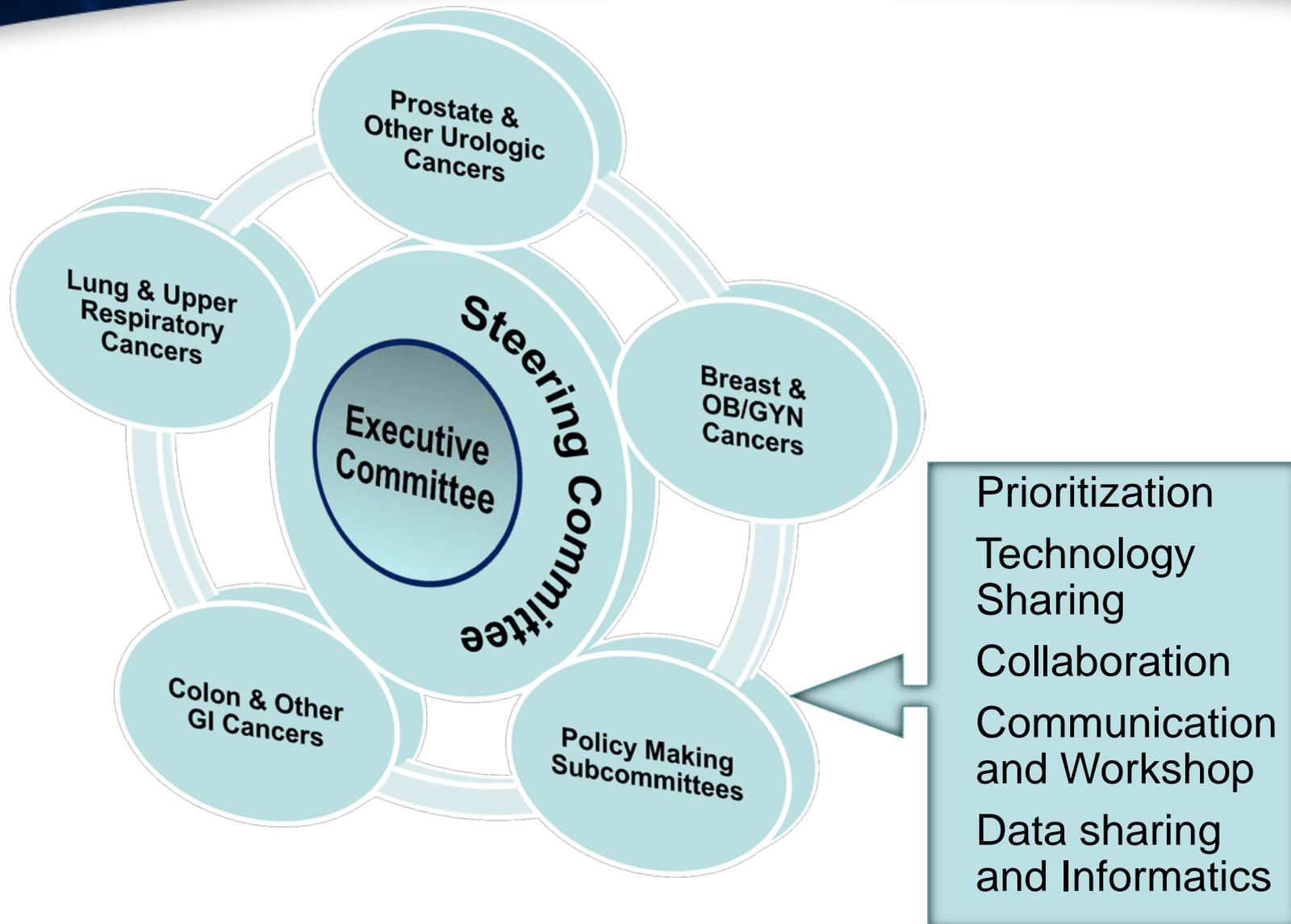
PD/PI: Collaborative Groups

PD/PI is a member and participates in a Collaborative Group*

- Breast and Gynecological Cancers
- Gastrointestinal Cancers
- Lung and Upper Aerodigestive Cancers
- Prostate and Genitourinary Cancers

* PI may participate in more than one Collaborative Group

EDRN Committees



**Early
Detection
Research
Network**



**EDRN
Informatics
Infrastructure**

Dan Crichton
Principal Computer Scientist and Program Manager
PI, EDRN Informatics Center
NASA Jet Propulsion Laboratory, Caltech
December 2, 2014



JPL

Jet Propulsion Laboratory
California Institute of Technology



JPL Serves as EDRN Informatics Center

- Development of an advanced EDRN Knowledge System to *capture* and *share* biomarker data results
- Leveraging/partnering between NASA-NCI in developing similar informatics capabilities in planetary and Earth science



Key Objectives of EDRN Informatics

- **Build enabling informatics infrastructure for collaboration, sharing and dissemination;**
- **Develop structured data collection, storage and curation for biomarker validation studies, biomarker database;**
- **Organize data that are searchable and informative;**
- **Integrate data from a variety of experimental platforms and laboratories in Knowledge Environment that is easily accessible.**

All activities are tailored toward making data verifiable, consistent and informative to community.

In 2000, EDRN investigators identified the following needs:

- Ability to develop informatics standards such as common data elements (CDEs) for biomarker research to allow for data to be linked together and analyzed
- Informatics to support multi-institutional validation studies
- Create tools to facilitate the use of the informatics standards for data collection (e.g. CDE Form Tool, EDRN Data Model, Public Portal)
- Ability to access specimens across EDRN Clinical validation Centers
- Ability to support secure data transfer, data analysis and communication
- Ability to support EDRN-wide data storage, curation and retrieval of multidimensional, multi-format data

EDRN Informatics Projects

EDRN has a number of focused projects that have been started in informatics to support the goals of capturing and sharing the state of biomarker research

Virtual Specimen Repository (ERNE): Access to information on specimens across EDRN;

EDRN-wide Portal: Access to EDRN-wide biomarker study results;

Science Data Warehouse (eCAS): Capture of biomarker data results from EDRN studies into a central repository. Security integrated.

Biomarker Database: Capture of biomarkers under study within the EDRN

Common Data Elements: Common sets of terms used to construct databases and forms

Laboratory Data Sharing (LabCAS): Enhance EDRN capabilities to automated the processing, capture and sharing of data from EDRN studies

Key Informatics Accomplishments

- Developed a **national, biomarker knowledge system** using advanced informatics technology
- Pioneered the concept providing **access to information** about **biospecimens** across EDRN at a national level (2001)
- Developed a **repository for capturing scientific data sets**; captured 90 data sets; integrated with the Canary Foundation infrastructure.
- Developed a **biomarker database** for capturing EDRN biomarkers; captured over 900 biomarkers
- Developed a **public portal** that provides **dissemination** of EDRN information as well as scientific data and results; over 2400 unique visitors a month
- Developing new tools for the Laboratory's to support the **processing, capture, curation and sharing of data** before publications
- Received NASA Award in 2011 for the “innovative use of NASA software technologies to support cancer research” due to **significant reuse of capability**.

Continuing DMCC/JPL Collaborations

Development of common data elements

- Negotiated with the EDRN investigators; Foundation for data capture
- Established a core ontology for cancer biomarker data

Development of shared databases

- Databases for site, member, protocol and other information

Development of EDRN knowledge-base

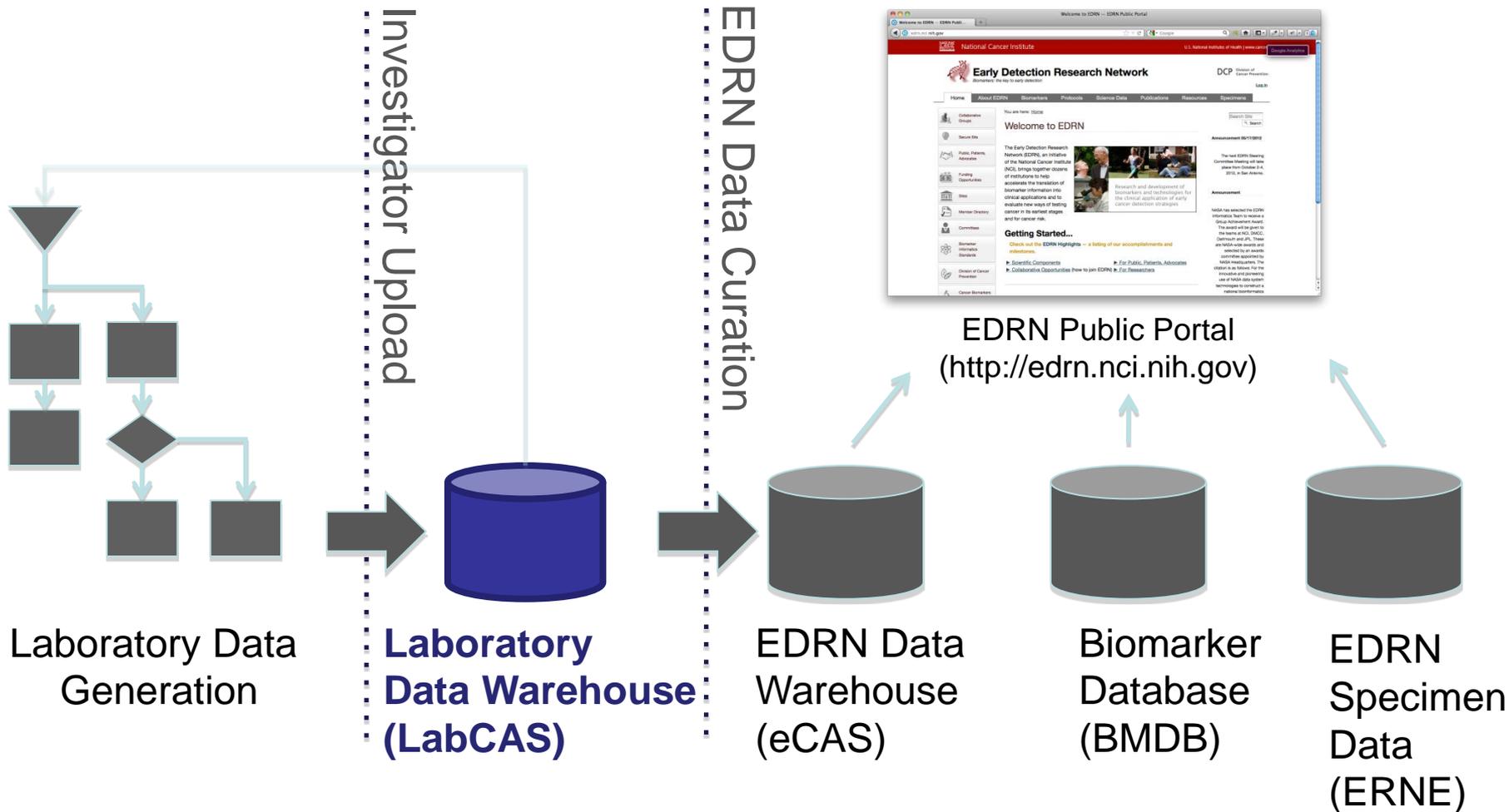
- Capture of the scientific data results from EDRN studies; to be discussed further
- Development of methods for curating and capturing data across EDRN

Coordinating on EDRN informatics tool development

Capturing and Sharing Biomarker Data Results

(2013+)

(2012)



LabCAS: Laboratory Catalog and Archive Service

- LabCAS is a new capability under development to provide investigators with a secure, reliable means to capture their **pre-publication** research datasets
- LabCAS also provides integrated data processing
- Enable investigators and collaborative groups/projects to share data in a secure manner as early as possible
- Scale to support data intensive projects



The screenshot shows the LabCAS website interface. At the top, there is a red header with the National Cancer Institute logo and the text "National Cancer Institute" and "U.S. National Institutes of Health | www.cancer.gov". Below the header, the "Early Detection Research Network" logo is displayed, along with the tagline "Biomarkers: The Key to Early Detection". The "DCP Division of Cancer Prevention" logo is also visible. A "Log In" link and the text "LABCAS" are in the top right corner. The main content area features a large image of green, rod-shaped bacteria with the text "LabCAS Laboratory Catalog and Archive Service" overlaid. Below the image, there are two columns of text: "What is LabCAS" and "More Information".

National Cancer Institute U.S. National Institutes of Health | www.cancer.gov

Early Detection Research Network DCP Division of Cancer Prevention

Biomarkers: The Key to Early Detection Log In

Home LABCAS

LabCAS
Laboratory Catalog and Archive Service

What is LabCAS

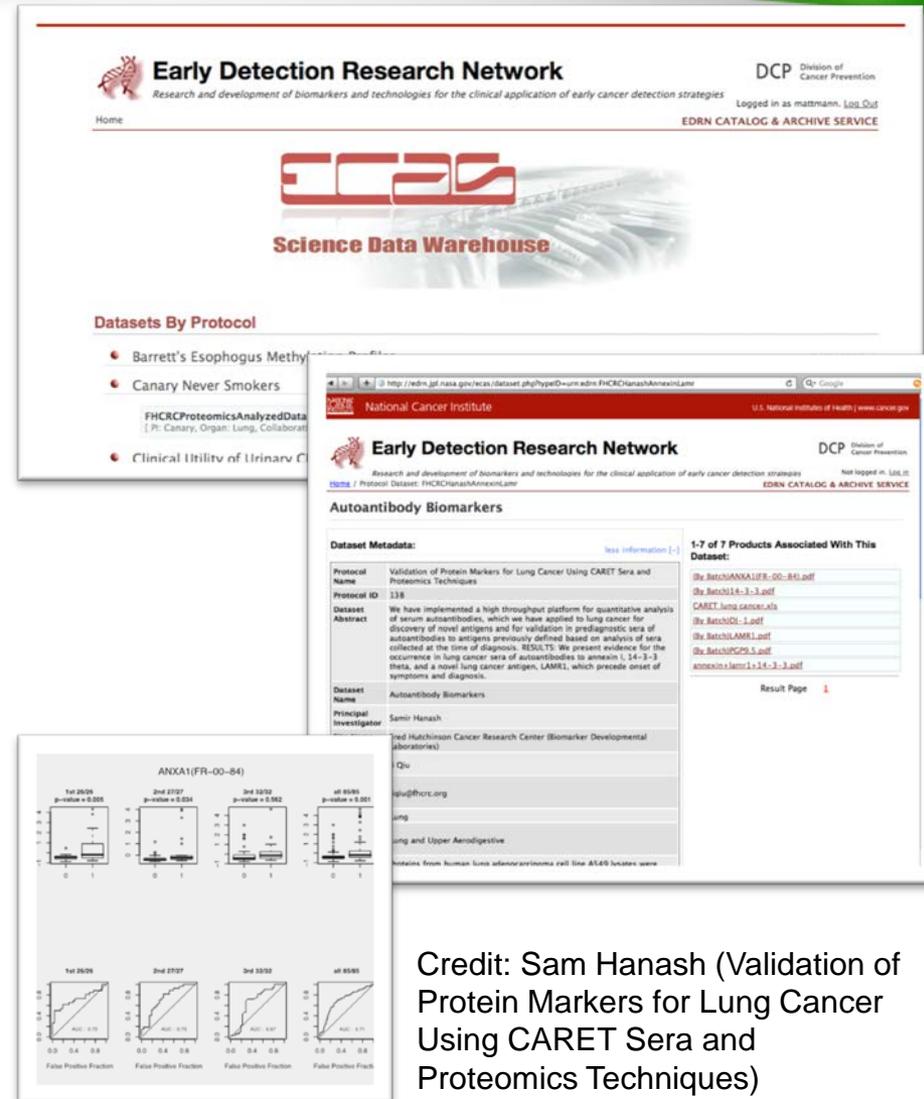
EDRN LabCAS is a better way to catalog and archive laboratory data files in a way that facilitates later retrieval and dissemination among collaborators.

More Information

LabCAS is currently under active development. For more information, please send an email to: edrn-proteome@jpl.nasa.gov.

eCAS: Capture and Sharing of Public Data Sets

- EDRN has a warehouse of public biomarker data for use today!
 - Uses the EDRN CDEs to populate a catalog describing the data sets
 - Supports public release/access to the data
 - Supports peer review of the data by collaborative groups prior to public release
 - Integrated with the rest of EDRN systems
- Provides a long term and central capture of EDRN study results for the broad community



Early Detection Research Network
Research and development of biomarkers and technologies for the clinical application of early cancer detection strategies
DCP Division of Cancer Prevention
Home | Protocol Dataset: FHCRCHanashAnnxin1Lamr | Logged in as mattmann, Log Out | EDRN CATALOG & ARCHIVE SERVICE

eCAS Science Data Warehouse

Datasets By Protocol

- Barrett's Esophagus Methylation Index
- Canary Never Smokers
- FHCRCHanashAnnxin1Lamr [P: Canary, Organ: Lung, Collaborator: ...]
- Clinical Utility of Urinary Cytology

Autoantibody Biomarkers

Dataset Metadata: [less information \[-\]](#)

Protocol Name: Validation of Protein Markers for Lung Cancer Using CARET Sera and Proteomics Techniques

Protocol ID: 138

Dataset Abstract: We have implemented a high throughput platform for quantitative analysis of serum autoantibodies, which we have applied to lung cancer for discovery of novel antigens and for validation in pre-diagnostic sera of autoantibodies to antigens previously defined based on analysis of sera collected at the time of diagnosis. RESULTS: We present evidence for the occurrence in lung cancer sera of autoantibodies to annexin 1, 14-3-3 beta, and a novel lung cancer antigen, LAMR1, which precede onset of symptoms and diagnosis.

Dataset Name: Autoantibody Biomarkers

Principal Investigator: Samir Hanash

Principal Investigator: Fred Hutchinson Cancer Research Center (Biomarker Developmental Laboratories)
C/O
sq@fhcr.org
Lung
Lung and Upper Aerodigestive

1-7 of 7 Products Associated With This Dataset:

- [fhcr/ANNA1/FR-00-84.pdf](#)
- [fhcr/14-3-3.pdf](#)
- [fhcr/lung_cancer_als.pdf](#)
- [fhcr/01-1.pdf](#)
- [fhcr/LAMR1.pdf](#)
- [fhcr/UPC/S.pdf](#)
- [annexin1amr114-3-3.pdf](#)

Result Page 1

ANXA1 (FR-00-84)

1st 2626 p-value = 0.005
2nd 2727 p-value = 0.034
3rd 3232 p-value = 0.062
all 8585 p-value = 0.001

1st 2626 AUC = 0.70
2nd 2727 AUC = 0.78
3rd 3232 AUC = 0.67
all 8585 AUC = 0.71

False Positive Fraction

Credit: Sam Hanash (Validation of Protein Markers for Lung Cancer Using CARET Sera and Proteomics Techniques)

eCAS: Access to Data

EDRN eCAS Web Portal
http://edrn.jpl.nasa.gov/ecas/dataset.php?typeID=urn:edrn:FHCRCHanashAnnexinLamr

National Cancer Institute U.S. National Institutes of Health | www.cancer.gov

Early Detection Research Network

DCP Division of Cancer Prevention

Research and development of biomarkers and technologies for the clinical application of early cancer detection strategies Not logged in. [Log in](#)

[Home](#) / Protocol Dataset: FHCRCHanashAnnexinLamr [EDRN CATALOG & ARCHIVE SERVICE](#)

Autoantibody Biomarkers

Dataset Metadata: [less information \[-\]](#)

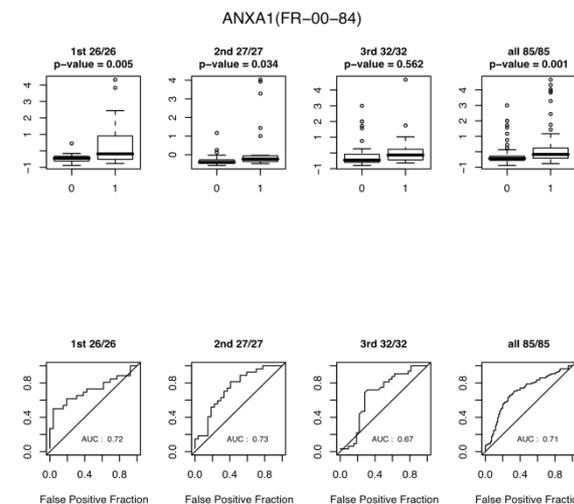
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- [CARET_lung_cancer.xls](#)
- [\(By Batch\)DJ-1.pdf](#)
- [\(By Batch\)LAMR1.pdf](#)
- [\(By Batch\)PGP9.5.pdf](#)
- [annexin+lamr1+14-3-3.pdf](#)

Result Page [1](#)

Download results



Credit: Sam Hanash (Validation of Protein Markers for Lung Cancer Using CARET Sera and Proteomics Techniques)

Biomarker Database: Capture of EDRN Biomarkers Under Research

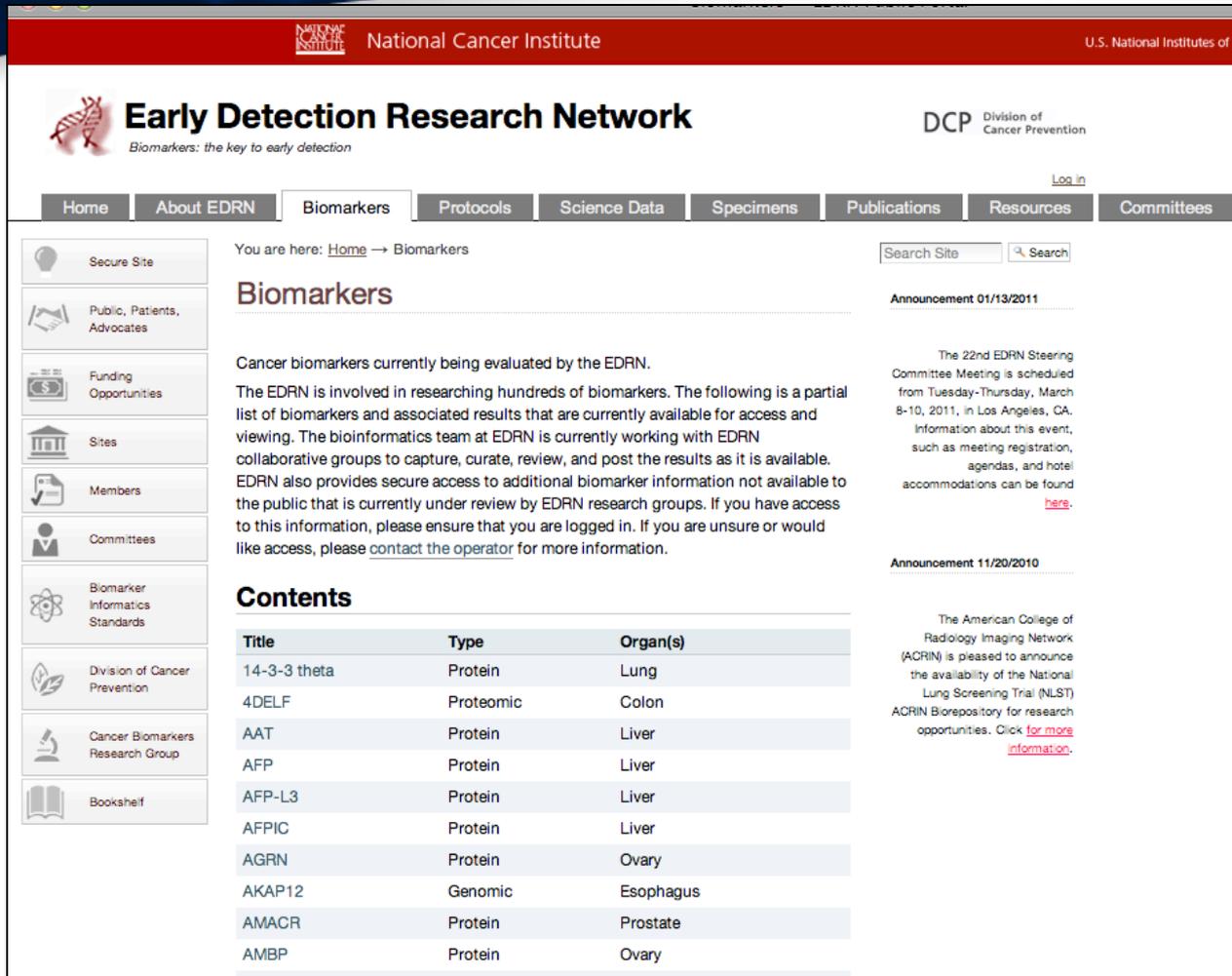
- **A database of annotated biomarkers that are either under development or reported in publications**
 - Over 900 biomarkers captured
 - Based on EDRN research

- **A national biomarker registry to track EDRN progress**
 - Similar to gene and protein type registries
 - Essential to tracking progress and supporting national collaboration of biomarker discovery and validation

- **Share results with the broader research community**

- **Integrate with existing databases (e.g., genomic, publication, etc. databases)**

EDRN Biomarker Database: Example



The screenshot shows the EDRN Biomarker Database website. At the top, there is a red header with the National Cancer Institute logo and name, and the text "U.S. National Institutes of Health". Below the header, the EDRN logo is displayed with the tagline "Biomarkers: the key to early detection". The main navigation menu includes "Home", "About EDRN", "Biomarkers", "Protocols", "Science Data", "Specimens", "Publications", "Resources", and "Committees". The "Biomarkers" tab is selected. The page content includes a search bar, a "You are here" breadcrumb, and a section titled "Biomarkers" with a paragraph of introductory text. Below this is a "Contents" table listing biomarkers with their titles, types, and associated organs. To the right of the table, there are two announcement sections with dates and brief descriptions of events.

National Cancer Institute U.S. National Institutes of Health

Early Detection Research Network
Biomarkers: the key to early detection

DCP Division of Cancer Prevention

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Home About EDRN **Biomarkers** Protocols Science Data Specimens Publications Resources Committees

You are here: [Home](#) → Biomarkers

Biomarkers

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Contents

Title	Type	Organ(s)
14-3-3 theta	Protein	Lung
4DELF	Proteomic	Colon
AAT	Protein	Liver
AFP	Protein	Liver
AFP-L3	Protein	Liver
AFPIC	Protein	Liver
AGRN	Protein	Ovary
AKAP12	Genomic	Esophagus
AMACR	Protein	Prostate
AMBP	Protein	Ovary

Search Site

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- Protocol
- Scientific Data
- Publications
- Additional Biomarker Resources

Example: Curation of a biomarker (14-3-3 theta)

14-3-3 theta — EDNR Public Portal

National Cancer Institute U.S. National Institutes of Health

Early Detection Research Network
Biomarkers: the key to early detection

DCP Division of Cancer Prevention

Log in

Home About EDNR Biomarkers Protocols Science Data Specimens Publications Resources Committees

You are here: [Home](#) → [Biomarkers](#) → 14-3-3 theta

Search Site Search

Announcement 01/13/2011

-  Secure Site
-  Public, Patients, Advocates
-  Funding Opportunities
-  Sites
-  Members
-  Committees
-  Biomarker Informatics Standards
-  Division of Cancer Prevention
-  Cancer Biomarkers Research Group
-  Bookshelf

14-3-3 theta

- Basics Organs Studies Publications Resources

Allases:

This biomarker is also known as:

14-3-3 protein T-cell, Protein HS1, 14-3-3 protein theta, tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, theta po, YWHAQ, 14-3-3 protein tau,

ATTRIBUTES

QA State: Accepted
Type: Protein
Short Name:

Description...

14-3-3 theta belongs to the 14-3-3 family of proteins which mediate signal transduction by binding to phosphoserine-containing proteins. This highly conserved protein family is found in both plants and mammals, and this protein is 99% identical to the mouse and rat orthologs. The 14-3-3 proteins have a wide range of ligands, are involved in a variety of biological pathways, and are known to be overexpressed in some human lung cancers, suggesting that they may play a role in tumorigenesis. 14-3-3 theta is an adapter protein implicated in the regulation of a large spectrum of both general and specialized signaling pathway. It binds to a large number of partners, usually by recognition of a phosphoserine or phosphothreonine motif. Binding generally results in the modulation of the activity of the binding partner. 14-3-3 theta antigens have been found to be targets of autoantibodies in subjects newly diagnosed with lung cancer.

Send this — Print this —

defined antigens. Investigation of 14-3-3 theta is ongoing.

Supporting Study Data

The following studies/protocols provide evidence supporting 14-3-3 theta indications for the Lung...

Validation of Protein Markers for Lung Cancer Using CARET Sera and Proteomics Techniques

1.1 To validate the finding from pilot studies with CARET sera of autoantibodies to annexins I and II and PGP9.5 as potential biomarkers for lung cancers before the clinical diagnosis, evaluating sensitivity and specificity by time before diagnosis, treatment arm, gender, histologic type, and smoking status. 1.2 To determine whether a pattern of occurrence of autoantibodies in lung cancer sera may be diagnostic of lung cancer that is not dependent on the occurrence of any particular autoantibody. 1.3 To compare the findings for individual biomarker candidates and combinations of biomarker candidates in participants who were current smokers versus former smokers.

[View more about this study](#)

Biomarker Characteristics Summary

Notes	Sensitivity	Specificity	Prevalence	NPV	PPV	Specific Assay Type
Individual sera collected from 85 subjects within a year prior to a diagnosis of lung cancer and 85 matched controls from the CARET cohort were used in this analysis. Sam	51.0	82.0	N/A	N/A	N/A	

- [Laboratories \(U01\)](#)
- [- Clinical Validation Centers \(U01\)](#)
- [- Biomarker Reference Laboratories \(U24\)](#)
- [- Data Management and Coordinating Center \(U24\)](#)

[EDRN Renewal flyer](#) NOTE- New receipt deadline for applications submitted for all EDNR FOAs is January 20, 2015, by 5:00 PM local time of applicant organization.

There will be a Pre-Application webinar to discuss each of the four individual EDNR FOAs on Tuesday, December 2nd, 2014, from 1pm-5pm (Eastern). Potential applicants interested in participating in the webinar should send a message to Dr. Sharmistha Ghosh (hoshianiqas@mail.nih.gov) no later than 5:00 p.m. (EST) November 21, 2014. Please mention the FOA of interest in the subject line.

Announcement 10/07/2014

EDRN Patient Advocates will host an EDNR Advocacy Educational Webinar, Biomarkers for Prostate Cancer Detection and Monitoring, on Monday, January 13th, 2015 at 1:00

Biomarker Database Content

928 individual biomarkers

Ten organs represented

- Bladder (2)
- Breast (165)
- Colon (13)
- Esophagus (11)
- Head & Neck (8)
- Liver (9)
- Lung (191)
- Ovary (205)
- Pancreas (7)
- Prostate (388)

- 27 biomarker “panels” or “signatures” included
- 68 biomarkers associated with multiple organs (e.g. information detailing *p16* activity in Esophagus, Lung and Prostate)
- Expert review completed in each Collaborative Group
- Markers from all four Collaborative Groups “Accepted” and released to public view

Research, Communicate, Curate, Annotate

Ability to locate specimens across EDRN

Clinical Centers: ERNE

- **Specimen Locator System, dubbed ERNE, EDRN Resource Network Exchange was developed to query data across EDRN's Clinical Validation Centers (CVC)**
- **The system is based on NASA JPL's Object-oriented Data module which can be easily tailored to the CVC's institutional informatics system**
 - Same software module used to share earth and planetary science data
- **ERNE allows the user to query the availability of specimens in real-time**
- **This is a first-ever system developed to query specimen on disparately distributed specimens across the country**
 - "ERNE" has been a model studied by many groups

Go To: [Home](#) > [JNCI](#) > [Archive](#) > [Vol. 95, No. 3](#) > Tenenbaum, pp. 186-187.

JNCI

*Journal of the
National
Cancer
Institute*

Journal of the National Cancer Institute, Vol. 95, No. 3, 186-187, February 5, 2003
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NEWS

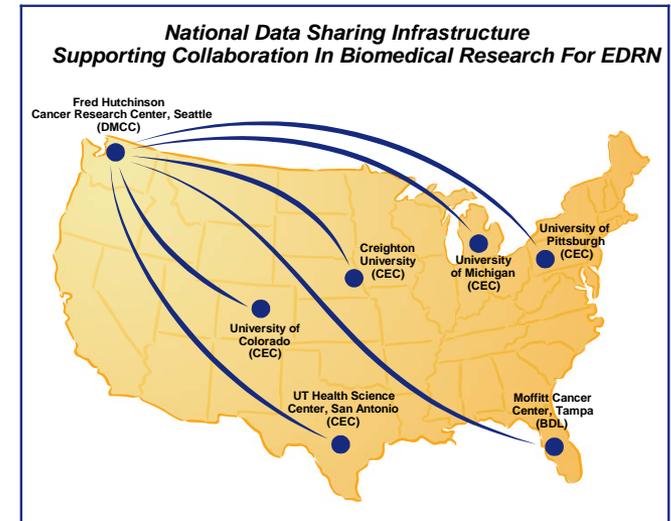
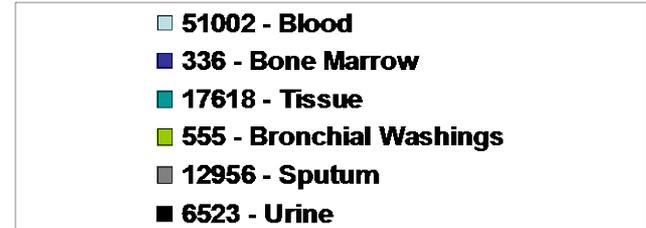
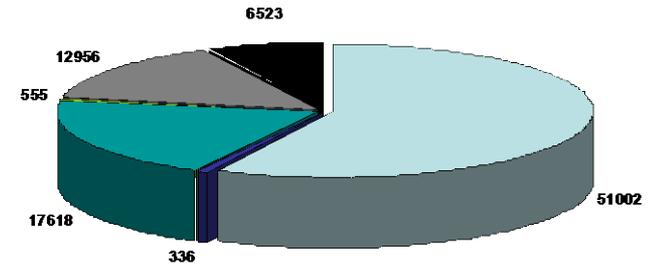
Serving Up Specimens: NASA-NCI Project Links Databases Across the Country

David Tenenbaum

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Participants in Virtual Specimen Bank

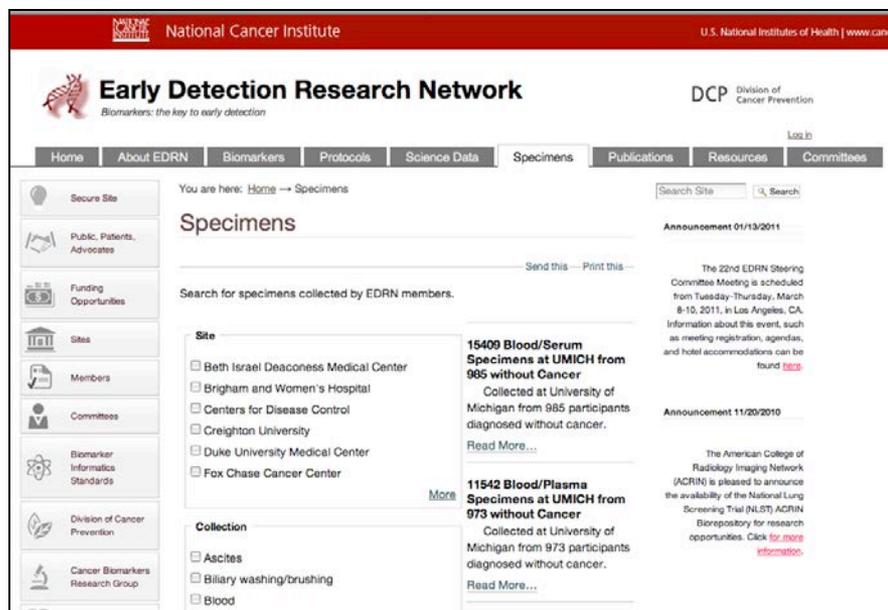
H. Lee Moffitt Cancer Center
University of Texas, San Antonio
Creighton University
University of Colorado
University of Pittsburgh
University of Michigan/Dartmouth University
(Great Lakes New England Consortium)
Brigham and Womens
MD Anderson
New York University
UCSD
Center for Disease Control
Johns Hopkins
Duke University
Fred Hutchinson Cancer Research Center
Fox Chase Cancer Research Center



ERNE – Example of query screen

EDRN Resource Network Exchange (ERNE)

- An *infrastructure* for sharing data resources across EDRN
- Supports *real time* (on demand) *distribution* of data to users
- Uses EDRN CDE Mapping Tool



National Cancer Institute U.S. National Institutes of Health | www.cancer.gov

Early Detection Research Network DCP Division of Cancer Prevention
Biomarkers: the key to early detection

Home About EDRN Biomarkers Protocols Science Data **Specimens** Publications Resources Committees

You are here: Home → Specimens

Search Site [Search]

Specimens

Search for specimens collected by EDRN members.

Site

- Beth Israel Deaconess Medical Center
- Brigham and Women's Hospital
- Centers for Disease Control
- Creighton University
- Duke University Medical Center
- Fox Chase Cancer Center

Collection

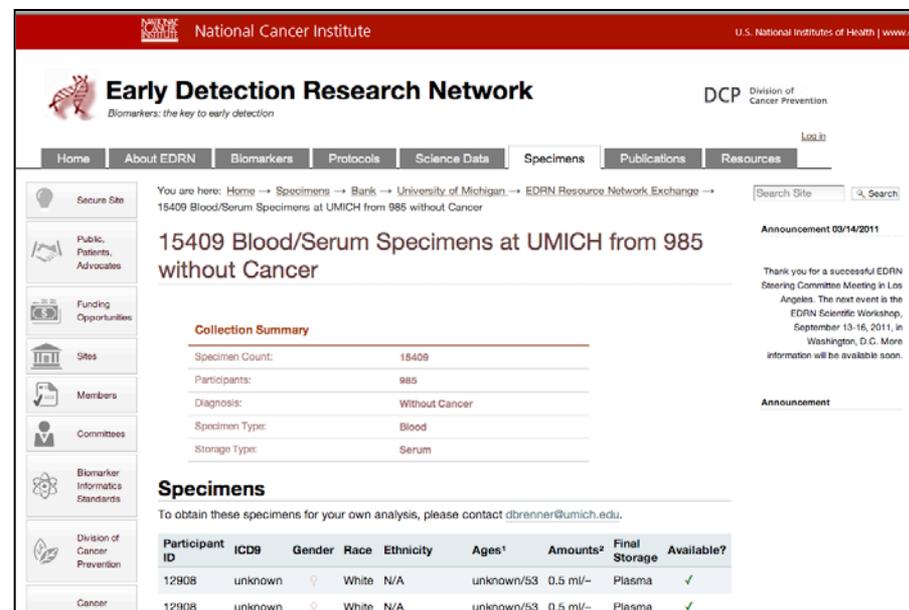
- Ascites
- Biliary washing/brushing
- Blood

15409 Blood/Serum Specimens at UMICH from 985 without Cancer
Collected at University of Michigan from 985 participants diagnosed without cancer.
Read More...

11542 Blood/Plasma Specimens at UMICH from 973 without Cancer
Collected at University of Michigan from 973 participants diagnosed without cancer.
Read More...

Announcement 01/13/2011
The 22nd EDRN Steering Committee Meeting is scheduled from Tuesday-Thursday, March 8-10, 2011, in Los Angeles, CA. Information about this event, such as meeting registration, agendas, and hotel accommodations can be found [here](#).

Announcement 11/20/2010
The American College of Radiology Imaging Network (ACRIN) is pleased to announce the availability of the National Lung Screening Trial (NLST) ACRIN Biorepository for research opportunities. Click [for more information](#).



National Cancer Institute U.S. National Institutes of Health | www.cancer.gov

Early Detection Research Network DCP Division of Cancer Prevention
Biomarkers: the key to early detection

Home About EDRN Biomarkers Protocols Science Data **Specimens** Publications Resources

You are here: Home → Specimens → Bank → University of Michigan → EDRN Resource Network Exchange → 15409 Blood/Serum Specimens at UMICH from 985 without Cancer

Search Site [Search]

15409 Blood/Serum Specimens at UMICH from 985 without Cancer

Announcement 03/14/2011
Thank you for a successful EDRN Steering Committee Meeting in Los Angeles. The next event is the EDRN Scientific Workshop, September 13-16, 2011, in Washington, D.C. More information will be available soon.

Announcement

Collection Summary

Specimen Count:	15409
Participants:	985
Diagnosis:	Without Cancer
Specimen Type:	Blood
Storage Type:	Serum

Specimens
To obtain these specimens for your own analysis, please contact dbrenner@umich.edu.

Participant ID	ICD9	Gender	Race	Ethnicity	Ages ¹	Amounts ²	Final Storage	Available?
12908	unknown	♀	White	N/A	unknown/53	0.5 ml/-	Plasma	✓
12908	unknown	♀	White	N/A	unknown/53	0.5 ml/-	Plasma	✓

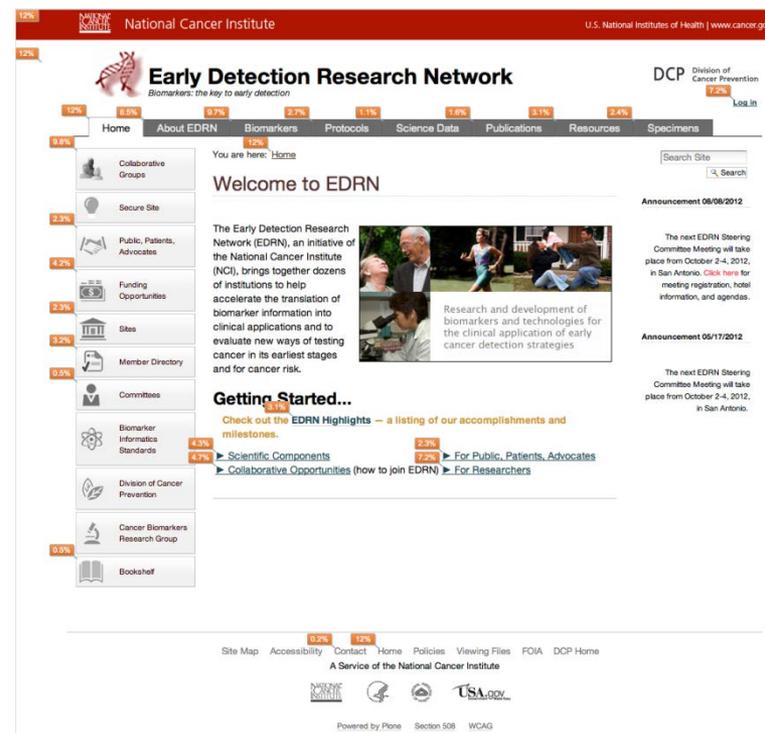
Public Portal

A one stop shop to access EDRN programmatic and science information

- Operated by NCI on the cancer.gov network
- Used by NCI and EDRN for disseminating program information
- Information spans from biomarker data all the way to member information
- Integrates information from the DMCC
- **Google-like search feature**

We have approximately 900 registered users and we get about 2400 unique visits a month

- A lot of ad hoc requests for data from outside EDRN



The screenshot shows the EDRN Public Portal website. At the top, it identifies the National Cancer Institute and the Division of Cancer Prevention (DCP). The main navigation bar includes links to Home, About EDRN, Biomarkers, Protocols, Science Data, Publications, Resources, and Specimens. A sidebar on the left provides quick access to various services and information, such as Collaborative Groups, Secure Site, Public, Patients, Advocates, Funding Opportunities, Sites, Member Directory, Committees, Biomarker Informatics Standards, Division of Cancer Prevention, Cancer Biomarkers Research Group, and Bookshelf. The main content area features a 'Welcome to EDRN' message, a brief description of the network's mission, and a 'Getting Started...' section with links to EDRN Highlights, Scientific Components, Collaborative Opportunities, and resources for Public, Patients, Advocates and Researchers. The footer includes a Site Map, Accessibility, Contact, Home, Policies, Viewing Files, FOIA, and DCP Home links, along with logos for the National Cancer Institute, the Division of Cancer Prevention, and the USA.gov logo.

EDRN Public Portal
(<http://edrn.nci.nih.gov>)

Accessing EDRN Data: Data may come from any of these sources

Early Detection Research Network
 Research and development of biomarkers and technologies for the clinical application of early cancer detection strategies.

14-3-3 theta

Validation of Protein Markers for Lung Cancer Using CARET Sera and Proteomics Techniques

PURPOSE: We have implemented a high-throughput platform for quantitative analysis of serum autoantibodies which we have applied to lung cancer for discovery of novel antigens, and for validation in pre-diagnostic sera of autoantibodies to antigens previously defined based on analysis of sera collected at the time of diagnosis. **MATERIALS AND METHODS:** Proteins from human lung adenocarcinoma cell line A549 lysates were subjected to extensive fractionation. The resulting 1524

Early Detection Research Network

Validation of Protein Markers for Lung Cancer Using CARET Sera and Proteomics Techniques

Abbreviated Name: Lung CARET

Description:

PURPOSE: We have implemented a high throughput platform for quantitative analysis of serum autoantibodies which we have applied to lung cancer for discovery of novel antigens, and for validation in pre-diagnostic sera of autoantibodies to antigens previously defined based on analysis of sera collected at the time of diagnosis. **MATERIALS AND METHODS:** Proteins from human lung adenocarcinoma cell line A549 lysates were subjected to extensive fractionation. The resulting 1524 factors were spotted in duplicate on nitrocellulose coated slides. The microarrays produced were utilized in a blinded validation study to determine whether annexin I, PDGF, and 14-3-3 theta antigens previously found to be targets of autoantibodies in newly diagnosed subjects with lung cancer are associated with autoantibodies in sera collected at the pre-symptomatic stage and to determine whether additional antigens may be identified in pre-diagnostic sera. Individual sera collected from 85

Early Detection Research Network

Science Data

Captured scientific data results from biomarker studies

The EDRN is involved in researching hundreds of biomarkers. The following is a partial list of associated results from biomarker research that are currently available for access and viewing. The bioinformatics team at EDRN is currently working with EDRN collaborative groups to capture, curate, review and post additional data as it is available. EDRN also provides secure access to additional biomarker information not available to the public that is currently under review by EDRN research groups. If you have access to this information, please ensure that you are logged in if you are unsure or would like access, please contact the operator for more information.

Title	PI(s)	Organ	Protocol	Collaborative Group
Autoantibody Biomarkers	Hanahaf, Samir	Validation of Protein Markers for Lung Cancer Using CARET Sera and Proteomics Techniques	Lung and Upper Aerodigestive	
Barnett's Esophagus Methylation Profile Dataset	Meltzer, Stephen	Barnett's Esophagus Methylation Profile	GI and Other Associated	

Biomarker Annotations

Protocols

Biomarker Data Results

Early Detection Research Network

Search results

15 matching resources (of 2 items)

All Results

- 334 Specimens at Centers for Disease Control
- 334 matching specimens at Centers for Disease Control, last modified Aug 03, 2010 01:54 PM
- Hanahaf 3-marker panel for Lung Cancer
- The EDRN validation study ("Validation of Protein Markers for Lung Cancer Using CARET Sera and Proteomics Techniques") presents evidence for the occurrence ... last modified Jul 23, 2010 01:16 PM - Reference: 576
- New York University School of Medicine
- Clinical Epidemiology and Validation Center last modified Jan 28, 2010 01:33 PM - Reference: 576
- Specimen Reference Sets
- Documentation, EDRN guidelines, and application forms for specimen reference sets last modified Jun 16, 2010 03:44 PM - Reference: 576
- 14-3-3 theta
- 14-3-3 theta belongs to the 14-3-3 family of proteins which mediate signal transduction by binding to phosphotyrosine-containing proteins. This highly conserved ... last modified Jul 23, 2010 01:16 PM - Reference: 576
- 9a-1
- 9a-1, also known as PARK-7, belongs to the peptidase C06 family of proteins. It acts as a positive regulator of androgen receptor-dependent transcription. It ... last modified Jul 23, 2010 01:16 PM - Reference: 576

Early Detection Research Network

Welcome to EDRN

The Early Detection Research Network (EDRN), an initiative of the National Cancer Institute (NCI), brings together scientists from across the nation to help accelerate the translation of biomarker information into clinical applications and to evaluate new ways of testing cancer for early stage and for cancer risk.

Getting Started...

- Scientific Components
- Collaborative Opportunities (How to Join EDRN)
- For Public Patients, Advocates
- For Researchers

Early Detection Research Network

Autoantibody Biomarkers

Dataset Metadata:

Protocol Name: Validation of Protein Markers for Lung Cancer Using CARET Sera and Proteomics Techniques

Protocol ID: 138

Dataset Abstract: We have implemented a high throughput platform for quantitative analysis of serum autoantibodies, which we have applied to lung cancer for discovery of novel antigens and for validation in pre-diagnostic sera of autoantibodies to antigens previously defined based on analysis of sera collected at the time of diagnosis. RESULTS: We present evidence for the occurrence in lung cancer sera of autoantibodies to annexin I, 14-3-3 theta, and a novel lung cancer antigen, LAMR1, which precede onset of symptoms and diagnosis.

1-7 of 7 Products Associated With This Dataset:

Product Name	Download Link
Validation of Protein Markers for Lung Cancer Using CARET Sera and Proteomics Techniques	(By: BarchANNAUER-00-86).pdf
14-3-3 theta	(By: Barch14-3-3-3).pdf
CARET Lung cancer.xls	(By: BarchDQ1-1.pdf)
Validation of Protein Markers for Lung Cancer Using CARET Sera and Proteomics Techniques	(By: BarchNCP9-1.pdf)
annexin I, 14-3-3 theta	(By: BarchNCP9-1.pdf)

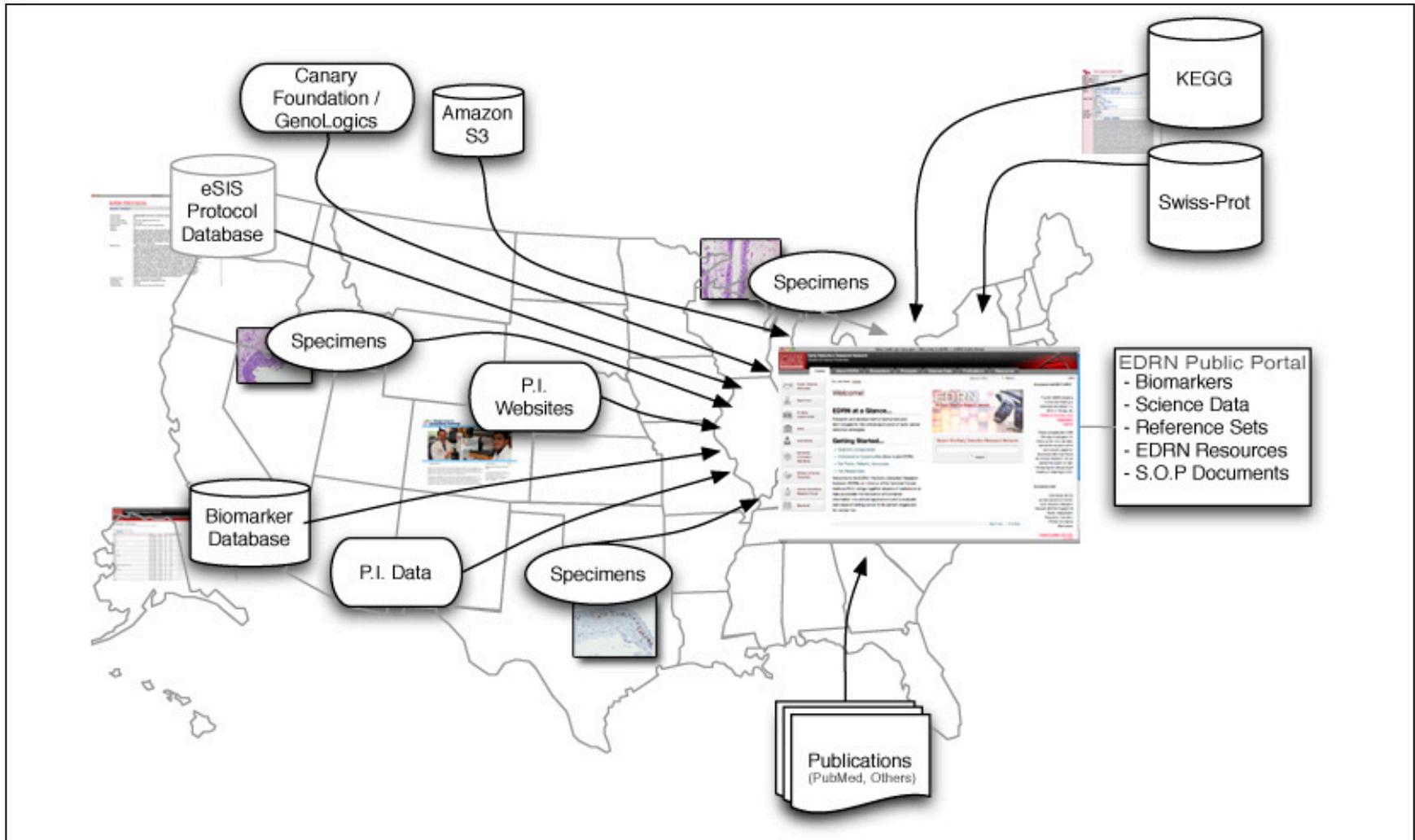
Specimens

Linked through Public Portal

Access to download data

What's Emerged...

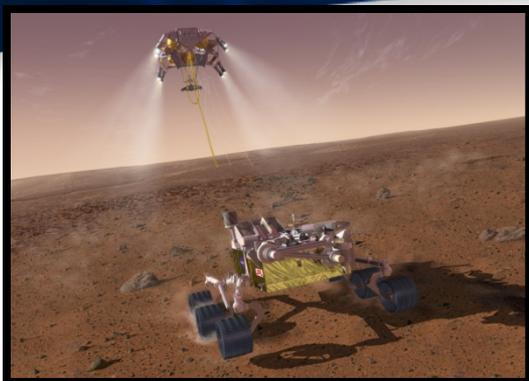
The EDRN Knowledge System



JPL and DMCC Responsibilities

- DMCC Responsibilities for EDRN Infrastructure
 - Prepare and produce data collection forms on biomarkers in collaboration with the EDRN IC;
 - Specify, capture and annotate EDRN scientific data from selected studies. Data for description and/or capture are at two levels: instrument (specific instruments at bench or in clinic, which generate EDRN biomarker data), and biomedical and clinical data at the database level;
 - Feed specifications back for integration into ontology models. Specifically, work on the development of metadata and review the ontology for the data captured at all levels of processing from the bench to the database to clinical work;
 - Collaborate with the EDRN IC to modify ontology models as needed;
 - Collaborate on common system designs or protocols with the IC and NCI, including methods and requirements for populating the databases and handling of data, including appropriate sharing of methods and data among collaborating organizations.
- JPL will work with the DMCC to organize the capture of content into the EDRN Knowledge System

Conclusion



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EDRN has a focused, leading-edge, informatics platform that can be leveraged today for sharing data.



http://twitter.com/edrn_ic

<http://www.facebook.com/group.php?gid=56938589930>

