Biomarkers for Early Detection and Diagnosis of Lung Cancer: An EDRN Biomarker Discovery Laboratory Experience

From the Thoracic Oncology Laboratory NYU Langone Medical Center New York, New York
Disclosures

• **Grants**: NCI EDRN, RO1, TCGA, DOD

• **Philanthropy**: Rosenwald Foundation, Stephen A. Banner Lung Cancer Foundation, Belluck and Fox, Levi, Phillips and Konigsberg, Simmons Foundation, Baron and Budd, multiple patients who shall remain anonymous

• **Industry**: Fujirebio, 20/20 Gene, MesoScale Diagnostics, Cynvezio, Source MDX, Celera, OPKO, SomaLogic, Genentech, Integrated Diagnostics, Transgenomics, Rosetta Genomics, Calithera, Pinpoint Genomics, Cizzle, Viomics, Myriad, VisionGate

• **Patents** (no money): osteopontin for diagnosis and prognosis of MPM; fibulin 3 for diagnosis and prognosis of MPM; mir-29c* for prognosis of MPM; mir-31 for diagnosis of MPM
The Early Detection Research Network

- Investigator-initiated infrastructure modeled after Cooperative Groups and established in 2000
- Collaborative and team science driven biomarker discovery, development and validation
- Built-in reward mechanisms for collaboration and team science
- Milestone-driven projects with incremental peer-review evaluation
- Inclusive infrastructure that solicits extramural investigators’ participation through a unique Associate Membership Program throughout the funding period
- Follows industrial/biotechnology standard practice for biomarker pipeline development
Organized into Collaborative Groups

https://edrn.nci.nih.gov/collaborative-groups
EDRN Structure is Based on Biomarkers Development Pipeline
EDRN Biomarker Pipeline

- Hundreds of biomarkers reviewed and evaluated
- More than 500 failed in rigorous testing
- More than 800 prioritized (EDRN Data Base)
- Many of them are in Phase II

https://edrn.nci.nih.gov/biomarkers
Collaborative Activities

- Extensive interactions; Monthly phone calls including scientific presentations, biomarker prioritization, guest speakers
- Two Steering Committee meetings each year combined with scientific workshop every 18 months; attended by non-EDRN members
- Dedicated Webpages for Each Collaborative Group
- More than 60 network-wide collaborative projects
- Partnerships with other NCI Programs, e.g. CPTAC, SPORES
National Resource

- Conducts multi-center, multidiscipline trials for biomarker validation
- Informatics and bioinformatic support for data collection, curation, storage and queries
- Centralized Statistical Center for data analysis and statistical support (DMCC);
- Fail-safe mechanism for efficient biomarker triaging for large, expensive validation studies (use of reference sets)
- Availability of large number of biospecimens (more than 100,000) using a uniform protocol
- Shared technologies on genomics, proteomics, and other ‘omics’ for collaborative studies
Collaborative Opportunity for Community and Public

- More than 200 Associate members, many of which are collaborating with EDRN members;
- Active partnership Foundations
  - Lustgarten Foundation N.Y.
  - Canary Foundation
- Collaboration with China (C-EDRN) and Cancer Research UK;
- EDRN Advocate Forum through quarterly Webinar.
Scientific Excellence

- Innovative Technologies, Study Designs and Approaches
- Biomarker Discovery
- Preanalytical Validation
- Analytical Validation

https://edrn.nci.nih.gov/network-consulting-team
## Clinical Assays in Use

<table>
<thead>
<tr>
<th>Detection/ Biomarker Assay</th>
<th>Discovery</th>
<th>Refine/ Adapt for Clin Use</th>
<th>Clinical Validation</th>
<th>Clinical Translation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood proPSA</td>
<td>√</td>
<td>✓</td>
<td>√</td>
<td>FDA approved</td>
</tr>
<tr>
<td>Urine PCA3</td>
<td>√</td>
<td>✓</td>
<td>√</td>
<td>FDA approved</td>
</tr>
<tr>
<td>Urine/TMA assay for T2S:Erg fusion for Prostate Cancer</td>
<td>√</td>
<td>✓</td>
<td>√</td>
<td>CLIA in process</td>
</tr>
<tr>
<td>FISH to detect T2S:Erg fusion for Prostate Cancer</td>
<td>√</td>
<td>✓</td>
<td>√</td>
<td>In CLIA Lab</td>
</tr>
<tr>
<td>Aptamer-based markers for Lung Cancer</td>
<td>✓</td>
<td>✓</td>
<td>√</td>
<td>In CLIA Lab</td>
</tr>
<tr>
<td>Proteomic Panel for Lung Cancer</td>
<td>✓</td>
<td>✓</td>
<td>√</td>
<td>In CLIA Lab</td>
</tr>
<tr>
<td>OVAI™ for Ovarian Cancer</td>
<td>✓</td>
<td>✓</td>
<td>√</td>
<td>FDA Approved</td>
</tr>
<tr>
<td>SOPs for Blood (Serum, Plasma), Urine, Stool, Vimentin Methylation Marker for Colon Cancer</td>
<td>✓</td>
<td>✓</td>
<td>√</td>
<td>Frequently used by biomarker research community</td>
</tr>
<tr>
<td>ROMA Algorithm for CA125 and HE4 Tests for Pelvic Mass Malignancies</td>
<td>✓</td>
<td>✓</td>
<td>√</td>
<td>FDA Approved</td>
</tr>
<tr>
<td>Blood/DCP and AFP-L3 for Hepatocellular Carcinoma</td>
<td>✓</td>
<td>✓</td>
<td>√</td>
<td>FDA Approved</td>
</tr>
<tr>
<td>Blood GP73</td>
<td>✓</td>
<td>✓</td>
<td>√</td>
<td>Together with AFP-L3 used in China for monitoring/risk assessment of cirrhotic patients for HCC</td>
</tr>
<tr>
<td>Bronchogen</td>
<td>✓</td>
<td>✓</td>
<td>√</td>
<td>In CLIA Lab</td>
</tr>
</tbody>
</table>
Is there a need for Early Detection/Diagnostic or Prognostic Biomarkers?

NYU Lung Cancer Progression/Survival Cohort
Patients (2006-2011) with Absolute Follow-up as of February 2013
Where do (blood) biomarkers fit in the natural history of mesothelioma and lung cancer?
# Thoracic cancer diagnostic biomarkers: The Necessary Steps to Believing a Biomarker

Sullivan-Pepe, JNCI 2001- EDRN

<table>
<thead>
<tr>
<th>Candidates</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Phase 4</th>
<th>Phase 5</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Discovery, Prediction</td>
<td>Assay validation</td>
<td>Retro-longitudinal</td>
<td>Prospective screening</td>
<td>Cancer Control</td>
</tr>
<tr>
<td>SERUM/PLASMA</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>MALDI TOF MS profiling</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SomaMers</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specific antigens/proteins</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>miRNA</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Challenges

- Who to screen? Risk group?
- How often should chest CT be offered?
- How to handle the high false positive rate (benign lung nodules)?
- How to streamline the Follow-up?
- Is it Cost effectiveness | implications
- How to implement for public policy
- What is the Impact on surgical | treatment approaches?
- Role(s) of molecular biomarkers?
What does it take to do this?

~ $600,000/year in salary costs
How do you orchestrate it?
How to quantitate how good a biomarker is: the ROC Curve

<table>
<thead>
<tr>
<th>Condition (as determined by &quot;Gold standard&quot;)</th>
<th>Precision = Σ True positive / Σ Test outcome positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Condition positive</td>
<td>False positive (Type I error)</td>
</tr>
<tr>
<td>Condition negative</td>
<td>True negative</td>
</tr>
</tbody>
</table>

Sensitivity = Σ True positive / Σ Condition positive
Specificity = Σ True negative / Σ Condition negative
Accuracy

Precision = Σ True positive / Σ Test outcome positive
Negative predictive value = Σ True negative / Σ Test outcome negative

TP  FP
FN  TN
1  1

P(TP) vs. P(FP)

0%  100%
How good should the biomarker be?

• Better than standard of care.
• What are the metrics?
  - Performance of the test: PPV & NPV
  - ROC curves (TPR vs FPR).
  - Net reclassification Improvement (NRI) index
  - Change in decision making.

Pecot, CEBP 2012
What do physicians want?

• A negative test result (that is, “benign”) to be correct with high probability (more than 90%) to ensure that malignant nodules are not accidentally eliminated
  • a high negative predictive value (NPV)
  • An NPV of 90% reduces the posttest probability of cancer to 10% or lower
    • That is a twofold reduction in cancer risk from the 20% pretest probability of cancer among patients selected for invasive procedures!

• The diagnostic test must be developed and validated on intended-use samples from multiple independent sites without demographic bias on key clinical parameters such as age, nodule size, and gender
  • Ideally in stage IA cancers.
  • The intended-use population should have a high occurrence of current and former smokers
What do patients or people at high risk or people with nodules want????

- They want their doctor to tell them with the least invasive way possible that either
  - You do not have to worry about having lung cancer
  - Your test tells us that something is brewing and we need to repeat the test over the next 3-6 months or longer
  - Your test tells us that the nodule you have on your CT scan is either definitely a cancer or definitely benign

THE LEAST INVASIVE WAY TO DO THIS IS BY LOOKING FOR SOMETHING IN THE BLOOD WITH A SIMPLE BLOOD DRAW!!!!
<table>
<thead>
<tr>
<th>Investigator</th>
<th>Site(s)</th>
<th>Platform/Expertise</th>
</tr>
</thead>
<tbody>
<tr>
<td>C. Croce</td>
<td>OSU BDL</td>
<td>MicroRNA and ultraconserved non-coding RNA</td>
</tr>
<tr>
<td>S. Dubinett</td>
<td>UCLA-Boston LC BDL</td>
<td>Genomics, microRNA, Central/Peripheral Airways; Role of Inflammation and biomarkers; RNASeq</td>
</tr>
<tr>
<td>A. Spira</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M. Lenburg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D. Elashoff</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D. Liebler</td>
<td>Vanderbilt BDL</td>
<td>Mass spec, LCMRM; shotgun proteomics; plasma/tissue</td>
</tr>
<tr>
<td>D. Taab</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P. Massion</td>
<td>Vanderbilt CVC</td>
<td>Case – control studies for diagnostic discovery; prospective CT imaging with collection of specimens; archive repository</td>
</tr>
<tr>
<td>H. Pass</td>
<td>North American Mesothelioma Consortium</td>
<td>Plasma/Tissue; Genomic, proteomic, glycomic, microRNA diagnosis and prognosis for mesothelioma; lung collaboration with W. Rom and industry</td>
</tr>
<tr>
<td>M. Huflejt</td>
<td></td>
<td></td>
</tr>
<tr>
<td>W. Rom</td>
<td>NYU CVC</td>
<td>Ongoing screening (1143) and r/o lung cancer (1047) prospective cohorts; collaborations with industry/H. Pass</td>
</tr>
<tr>
<td>D. Sidransky</td>
<td>Hopkins BDL</td>
<td>Epigenetic/methylation markers serum, plasma, sputum, BAL</td>
</tr>
<tr>
<td>S. Stass</td>
<td>U. Maryland Biomarker Reference laboratory</td>
<td>Analytic and Clinical Validation of lung biomarkers; microRNA for early detection/standardization of qPCR techniques</td>
</tr>
</tbody>
</table>

BDL CVC BRL
Early Detection/Diagnostic/Prognostic Blood Based Platforms: Mesothelioma and Lung Cancer

- **Proteomic**
  - Serum
    - MRM-Mass Spec
      - Indie Diagnostics
    - SomaMers
      - SomaLogic
  - Plasma
    - Osteopontin
    - Luminex
    - Autoantibodies

- **MicroRNA**
  - Plasma
    - Croce et al
  - Exosomes
    - Cazzoli et al

- **Multiple Reaction Monitoring Mass Spectroscopy proteomics**
  - Nucleotides constructed to bind to specific proteins and to remain bound during various manipulations
  - Short “noncoding” ~22 nucleotides in length after processing, double-stranded,
  - Bind 3’-UTR of target transcripts, leading to:
    - Ribosomal interference
    - Degradation of transcript
  - May act as oncogenes or TSGs
  - Very stable in plasma/serum/FFPE

- **microvesicles specialized in the transport of different types of RNA in particular microRNAs**
A Blood-Based Proteomic Classifier for the Molecular Characterization of Pulmonary Nodules: Indie Diagnostics

- Shotgun Proteomic analysis of tumors.
- Selected candidate proteins for testing in the blood

**Steps in refining the 388 candidates down to the 13-protein classifier.**

<table>
<thead>
<tr>
<th>Number of proteins</th>
<th>Refinement</th>
</tr>
</thead>
<tbody>
<tr>
<td>388</td>
<td>Lung cancer-associated protein candidates sourced from tissue and literature</td>
</tr>
<tr>
<td>371</td>
<td>Number of the 388 protein candidates successfully developed into an MRM assay</td>
</tr>
<tr>
<td>190</td>
<td>Number of the 371 MRM protein assays detected in plasma</td>
</tr>
<tr>
<td>125</td>
<td>Number of the 190 MRM protein assays detected in at least 50% of cancer or 50% of benign discovery samples</td>
</tr>
<tr>
<td>36</td>
<td>Number of the 125 detected proteins that were cooperative</td>
</tr>
<tr>
<td>21</td>
<td>Number of the 36 cooperative proteins with robust MRM assays (that is, no interfering signals, good signal-to-noise ratios, etc.)</td>
</tr>
<tr>
<td>13</td>
<td>Number of the 21 robust and cooperative proteins with stable logistic regression coefficients</td>
</tr>
</tbody>
</table>

- Developed 13 multiple reaction monitoring MRM assays. LRP1, BGH3, COIA1, TETN, TSP1, ALDOA, GRP78, ISLR, FRIL, LG3BP, PRDX1, FIBA, GSLG1
- Training and testing algorithm.

**Peptide** | **Protein** | **Location**
-------------|-------------|-------------
LRP1 | Prolow-density lipoprotein receptor-related protein 1 | Secreted |
BGH3 | Transforming Growth factor beta induced protein 3 | Secreted |
COIA1 | Collagen alpha-1(XVIII) chain | Secreted |
TETN | Tetraneclin | Secreted |
TSP1 | Thrombospondin-1 | Secreted |
ALDOA | Fructose-bisphosphate aldolase A | Secreted |
GRP78 | 78 kDa glucose-regulated protein | Endoplasmic reticulum |
ISLR | Immunoglobulin superfamily containing leucine-rich repeat protein | Secreted |
FRIL | Ferritin light chain | Secreted |
LG3BP | Galectin-3-binding protein | Secreted |
PRDX1 | Peroxiredoxin-1 | Cytoplasm |
FIBA | Fibrinogen alpha chain | Secreted |
GSLG1 | Golgi apparatus protein 1 | Golgi membrane |

Li et al. Sci Transl Med. 2013 Oct
13 MRM predictor of lung cancer among 247 lung nodules 4-30 mm (prevalence 15%)

A negative test implies a >2 fold decrease risk for cancer.

High NPV of the test would obviate 1/4 patients with benign nodules from a biopsy.

IF THE TEST SCORE IS 0.8 OR HIGHER, THEN THE CHANCE OF THE NODULE BEING BENIGN IS 90% OR MORE!!!!

Li et al. Sci Transl Med. 2013 Oct
SomaLogic Slow Off Rate Modified Aptamers (SOMA) Platform
## The SomaLogic Proteomic Platform: Modified Aptamer Technology

<table>
<thead>
<tr>
<th><strong>Metric</strong></th>
<th><strong>Conditions</strong></th>
<th><strong>Result</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>Median LLOQ</td>
<td>$\sim 0.3 \text{ pM}$</td>
</tr>
<tr>
<td>Dynamic Range</td>
<td>Over all proteins in plasma or serum</td>
<td>$10^7$</td>
</tr>
<tr>
<td></td>
<td>Each aptamer at one dilution</td>
<td>$\sim 10^4$</td>
</tr>
<tr>
<td>Precision</td>
<td>Median inter-run CV</td>
<td>$5%$</td>
</tr>
<tr>
<td>Sample Volume</td>
<td>Per sample, for $&gt;800$ proteins and $\sim 25$ controls</td>
<td>$8 \text{ uL}$</td>
</tr>
<tr>
<td>Multiplex Size</td>
<td>Current $#$ unique human proteins per sample</td>
<td>$1034$</td>
</tr>
<tr>
<td>Time to result</td>
<td>Automated assay &amp; hybridization detection</td>
<td>$\sim 30$ hours</td>
</tr>
<tr>
<td>Throughput</td>
<td>One robot, 2.5 FTEs</td>
<td>168 samples/day</td>
</tr>
</tbody>
</table>

$>1$M analytes/week

*PLoS One. 2010 Dec 7;5(12):e15003*
Total n = 1326
291 Cases
1035 Controls

Biomarker Selection
Algorithm Training & Cross Validation

Blinded Algorithm Verification

213 Cases
772 Controls
78 Cases
263 Controls

AUC = 0.91
AUC = 0.90

---

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>UniProt ID</th>
<th>Direction*</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cadherin-1</td>
<td>P12830</td>
<td>down</td>
<td>cell adhesion, transcription regulation</td>
</tr>
<tr>
<td>CD30 Ligand</td>
<td>P32971</td>
<td>up</td>
<td>cytokine</td>
</tr>
<tr>
<td>Endostatin</td>
<td>P39060</td>
<td>up</td>
<td>inhibition of angiogenesis</td>
</tr>
<tr>
<td>HSP 90α</td>
<td>P07903</td>
<td>up</td>
<td>chaperone</td>
</tr>
<tr>
<td>LRIG3</td>
<td>Q6UXW1</td>
<td>down</td>
<td>protein binding, tumor suppressor</td>
</tr>
<tr>
<td>MIP-4</td>
<td>P55774</td>
<td>up</td>
<td>monokine</td>
</tr>
<tr>
<td>Pleiotrophin</td>
<td>P21246</td>
<td>up</td>
<td>growth factor</td>
</tr>
<tr>
<td>PRKCI</td>
<td>P41743</td>
<td>up</td>
<td>serine/threonine protein kinase, oncogene</td>
</tr>
<tr>
<td>RGM-C</td>
<td>Q6ZVN8</td>
<td>down</td>
<td>iron metabolism</td>
</tr>
<tr>
<td>SCF sR</td>
<td>P16721</td>
<td>down</td>
<td>decoy receptor</td>
</tr>
<tr>
<td>s-L-Selectin</td>
<td>P14151</td>
<td>down</td>
<td>cell adhesion</td>
</tr>
<tr>
<td>YES</td>
<td>P07947</td>
<td>up</td>
<td>tyrosine kinase, oncogene</td>
</tr>
</tbody>
</table>
Osteopontin Plasma Levels in Early Stage NSCLC

- Plasma OPN elevated in early stage NSCLC compared to smokers without cancer
- Plasma OPN levels decrease in response to resection
- Preliminary evidence for rise in plasma OPN with recurrence
- But.....what about longitudinal studies????????

Blasberg, J. JCO, Feb 2010.
1182 subjects; 3771 CT scans with 2174 matched plasma samples.
Twenty-six NSCLC have been detected since 2001:
- 10 prevalence cancers
- 16 incident cancers.

Prevalent Cancers

Incident Cancers

Never Developed Cancer
Nested case-control study to evaluate plasma OPN as a diagnostic biomarker for NSCLC within this screening cohort.

- Prevalence cancers were excluded
- Incident cancers with serially banked plasma and 1-4 matched controls for each cancer were identified.
- Matched for age, sex, pack years, and the duration of the surveillance interval over which plasma samples were collected.
- Controls were considered free of cancer due to lack of clinical progression on CT screening for an interval of at least 24 months following evaluated surveillance interval.
MicroRNA signatures in tissues and plasma predict development and prognosis of computed tomography detected lung cancer: Boeri and C. Croce, OSU

• Objective:
  • Measure plasma mirs which can pre-diagnose CT detected lung cancer, as well as diagnose lung cancer at the time of CT detection.

• Methods:
  • Two large Italian lung cancer screening programs (28 cancers and 53 cancers)
    • One for discovery and the other for validation.
  • Use microfluidic cards to determine top 100 microRNA profiles of pre-diagnostic (>1y) and diagnostic plasmas
  • For normalization, mirs were expressed as ratios to each other and normalized to plasmas from individuals not developing lung cancer.

RESULTS

PreDiagnosis: 16 ratios/15 miRNAs discriminated developing lung cancer (80% sp, 90% se); Validation had a sensitivity of 80% and specificity of 90% (AUC-ROC = 0.85, P < 0.0001)

Diagnosis: 16 ratios/13 miRNAs classified lung cancer (80% sp, 84% se); Validation had a sensitivity of 75% and a specificity of 100% (AUC-ROC = 0.88, P < 0.0001)

Prognosis: 10 ratios/9 miRNAs, identified poor prognosis (dead or with progressive disease) with 100% sensitivity and 100% specificity, and in the validation set, the sensitivity of this signature was 80% with 100% specificity.

Plasma Exosomes for Screening and Diagnosis

J. Thorac. Oncol. 2013;8: 1156-1162
Plasma Exosomes: Population and Results

### Variable

<table>
<thead>
<tr>
<th>Study set</th>
<th>Adenocarcinomas (n = 50)</th>
<th>Granulomas (n = 30)</th>
<th>Healthy (n = 25)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 10)</td>
<td>(n = 10)</td>
<td>(n = 10)</td>
<td></td>
</tr>
</tbody>
</table>

- **Age, mean ± SD**
  - Adenocarcinomas: 66.1 ± 14.0
  - Granulomas: 64.8 ± 13.7
  - Healthy: 65.6 ± 7.4
  - p = 0.971

- **Sex, n (%)**
  - Male: 3 (30.0%)
  - Female: 7 (70.0%)
  - p = 0.861

- **Smoking habit, n (%)**
  - Yes: 5 (50.0%)
  - No: 5 (50.0%)
  - p = 0.024

- **Nodule size, mean ± SD**
  - Adenocarcinomas: 1.42 ± 0.24
  - Granulomas: 1.34 ± 0.56
  - p = 0.683

### Test Results

### Screening Test

- **Sensitivity:** 97.5%
- **Specificity:** 72%
- **Positive Predictive Value:** 92%
- **Negative Predictive Value:** 90%
- **AUC ROC:** 90.8

### Diagnostic Test

- **Sensitivity:** 96%
- **Specificity:** 80%
- **AUC ROC:** 76

*One-way ANOVA test.
χ² test.
Student's t test for unpaired data.
ANOVA, analysis of variance.
Clinical utility of a diagnostic biomarker: study design

Randomization of nodules based on the use of a biomarker test.
Proves that biomarker “+” affects patients outcome
Proves that biomarker test affects patients outcome when compared with unselected use of same Standard Of Care.

**Outcomes:**
- Early stage
- Futile Thorac.
- Survival
- Decrease cost

Randomize IPNs

Positive → Biopsy

Negative → 3 mo CT F/U

SOC (Guidelines)

No test → Biopsy

3 mo CT F/U
Thanks to…

• NYU Thoracic Lab
  • Chandra Goparaju PhD
  • Jessica Donington MD
  • Ryan Harrington BS
  • Amanda Beck BS
  • Joe Levin BS
  • Nathalie Hirsch BA

• Mt. Sinai Selikoff Foundation
  • Stephen Levin MD

• Carbone Laboratory, University of Hawaii
  • Michele Carbone MD, PhD
  • Haining Yang, PhD

• University of Toronto
  • Ming-Sound Tsao MD
  • Geoffrey Liu MD

• Ohio State University
  • Carlo Croce MD
  • Stefano Volina PhD

• Industrial Partners
  • Indie Diagnostics
  • SomaLogic
  • Fujirebio

• Karmanos Cancer Institute
  • Anil Wali PhD

• Early Detection Research Network, NCI, NIH
  • DMCC
    • Mark Thornquist PhD

• Lung Cancer Foundation of America/IASLC

…..and of course all the patients and volunteers who contributed specimens so this could be done