

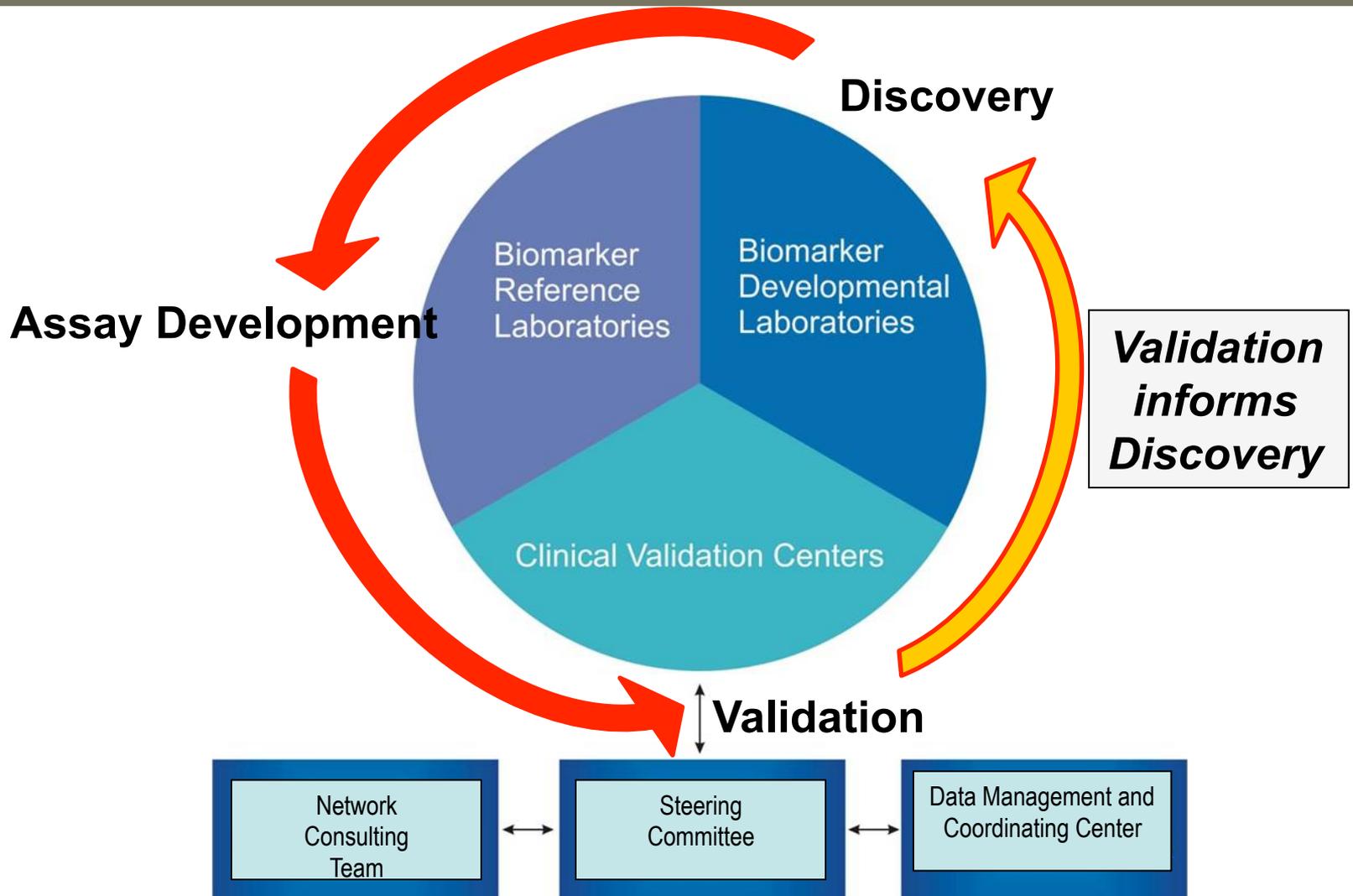
Early Detection Research Network: Validation Infrastructure

*Jo Ann Rinaudo, Ph.D.
Division of Cancer Prevention*

Mission

The NCI Early Detection Research Network's (EDRN) mission is to implement biomarker research through strategic and systematic, evidence-based discovery, development and validation of biomarkers for cancer risk assessment, early detection, diagnosis, and prognosis of cancer.

Organization of EDRN



Phases of Biomarker Development

<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>

Biomarker Validation Trials

- Demonstrate that the biomarker or panel of biomarkers accurately and reliably distinguishes individuals with cancer from those that do not have cancer.
- Requires a robust assay method and well characterized and processed clinical specimens collected at multiple sites.
- Assays performed at a site which is blinded to type of specimens.

Clinical Validation Centers

- **Conduct Biomarker Validation Studies**
- **Serve as a Collaborative Resource for the Network**
- **Partner with EDRN Biomarker Discovery/ Developmental Laboratories (BDLs) and Biomarker Reference Laboratories (BRLs)**

Biomarker Validation Studies

- **CVCs conduct biomarker validation studies using markers identified by the discovery laboratories.**
- **Conduct clinical research on the validation of biomarkers for early cancer detection and risk assessment. This research must conform to defined Phase 2 or Phase 3 biomarker studies.**

Good supporting evidence for the proposed biomarker(s).

Phase 2 and Phase 3 Biomarker Studies

- **Phase 2 studies**

- Ability of biomarkers to distinguish people with cancer from those without, or
- Determine accuracy of biomarkers to predict progression from a precancerous lesion to cancer.

- **Phase 3 studies**

- Assess the capacity of a biomarker to detect preclinical disease by testing the marker against specimens collected longitudinally from research cohorts.

Characteristics of Biomarker Validation Trial

- Led by initiating PI
- Addresses a clinically significant problem
- Based on solid preliminary data
- Protocol driven
- Multi-center
- Coordinated by Data Management and Coordinating Center
- Web based data submission

Applying for a Biomarker Validation Trial

1. Submit a biomarker validation proposal to the NCI Program Staff.
2. Proposal is evaluated by the appropriate EDRN Collaborative Group, external reviewers, and the EDRN Steering Committee.
3. If approved, the PI will work with the Data Management and Coordinating Center to develop a protocol and manual of operations. To the extent possible, other EDRN CVCs and BRLs can participate in the trial.

Clinical Validation Trials

- Prostate cancer – [-2]proPSA (FDA approved)
- Prostate cancer – PCA3 (FDA approved)
- Ovarian cancer – HE4 and CA125 and ROMA (FDA Approved)
- Ovarian cancer – Protein marker panel (FDA approved)
- HCC – DCP [Wako, industry partner] (FDA approved)
- Bladder cancer – MSA (negative findings)
- Colon cancer – DNA methylation and protein markers
- Mesothelioma – SMRP Validation

Prospective Specimen Collections / Reference Sets

Specimens can be collected prospectively to support:

- Validation studies;
- Reference Set collections;
- Requests from other EDRN investigators;
- Collaborations with ongoing trials.

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

MCL and EDRN Collaborations

- **Collection of biospecimens / reference sets**
- **Serve as a resource for validation studies**
- **Partner with discovery and reference laboratories for optimization of biomarker(s)**
 - Robust assay development
 - Well characterized clinical specimens
- **Support for initiation of validation studies for biomarkers identified by MCL consortium investigators**

Thank You!

