CLINICAL PROTEOMIC TECHNOLOGIES FOR CANCER

Clinical Proteomic Technologies Initiative for Cancer

Pre-Application Meeting

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National Cancer Institute

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NATIONAL CANCER INSTITUTE

Molecular Oncology: NCI's Strategy and Strategic Initiatives

CLINICAL PROTEOMIC TECHNOLOGIES FOR CANCER

- Sustain and Enable Basic Research, Discovery and Innovation
- Deal with the Data Deluge – Connect the Enterprise – Bioinformatics
- Provide Common Research Infrastructure – Biospecimens, Genomics, Proteomics/Biomarkers
- Apply, Provide, Leverage Advanced Technologies – Advanced Imaging, Nanotechnology, Systems Biology
- Optimize Clinical Trials for the New Science
- Ensure Delivery, Outcomes Research, Economic Models
- Build Science-Based Partnerships with Regulatory Bodies, Foundations and Industry

Enabling Individual and Large-Scale Post Genomics Translational Research

CLINICAL PROTEOMIC TECHNOLOGIES FOR CANCER

- **Basic Infrastructure**
  - Bioinformatics – caBIG™
  - Biospecimens – biobanks
  - Clinical Research
    - CTWG
- **Common Technology Platforms**
  - Biomarkers – Proteomics*
  - Human Cancer Genome Pilot Project
- **Advanced Technologies**
  - Advanced Imaging
  - Nanotechnology*
- **Integrated, Multidisciplinary Teams, Networks and Partnerships**

The Promise of Biomarkers for Molecular Oncology

CLINICAL PROTEOMIC TECHNOLOGIES FOR CANCER

New target discovery (understand underlying biology)

Drug development – markers of toxicity, metabolism, etc.

Early detection (broad or specific detection / corroboration of specific disease stage)

Identify molecular basis of disease phenotypes

Assessment of disease aggressiveness

Rational choice of treatments

Assessment of treatment effectiveness

Prevention markers

Potential of Proteomics

Evidence suggests that measurements of proteins and peptides may represent reliable indicators of aberrant cellular processes associated with cancer.

An integrated, systematic approach is needed to apply proteomic technologies and resources to solve mission-critical problems in cancer research.

Potential of Proteomics

Proteomic technologies offer the potential opportunity to enable:

- Early detection
- Molecular imaging probe and sensor development
- Discovery of targeted drugs
- Rationally developed clinical trials
  (e.g., stratification, intermediate endpoints)

Proteomics – Major Barriers to Sensitivity, Reproducibility and Discovery*

(No technology currently interrogates more than 1% of the proteome)

CLINICAL PROTEOMIC TECHNOLOGIES FOR CANCER

Gel Based

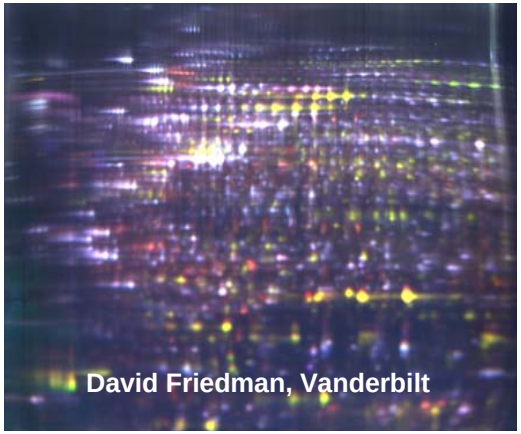
- 2-D Gel electrophoresis
- LC / LC / Gel electrophoresis

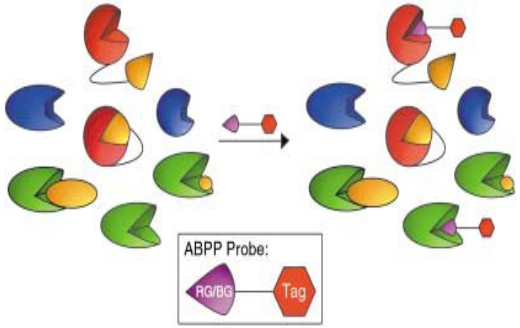
Mass Spectrometry Based

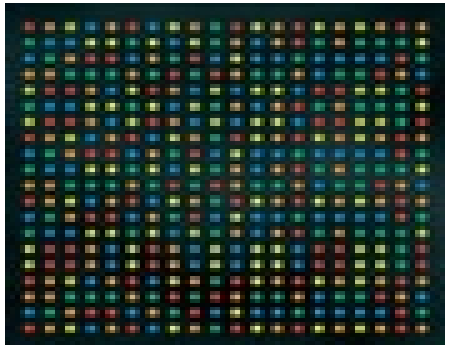
- LC proteins – MS / MS protease derived peptides
- LC / MS / MS – complex peptide mixtures
- MALDI MS – direct tissue analysis, activated surfaces

Chip / Array Based

- Antibody probes
- Activity based probes
- Chemically activated surfaces







No Lack of Standards – Everyone Has One

**Slide from Richard Caprioli*

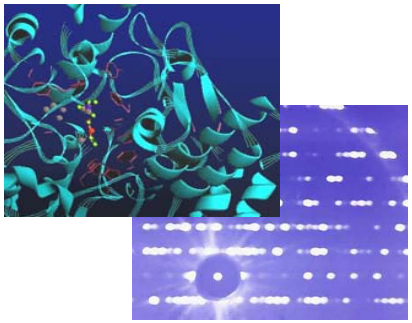
NCI Process for Community Input

April 2002	**Proteomics Planning Workshop *(NCI/NHGRI/NIGMS)*** Bethesda, Maryland
April 2003	**Proteomic Technologies for Early Cancer Detection** Chantilly, Virginia
June 2004	**Initial draft proposal for a Clinical Proteomics/Biomarker Discovery Initiative**
Sept 2004 Nov 2004	**Clinical Proteomics and Biomarker Discovery in Cancer Research** East Coast – Bethesda, Maryland West Coast – Menlo Park, California
Jan 2005	**Clinical Proteomics Technologies Team Initiative proposal**
Feb 2005	**Proteomic Technologies Informatics Workshop** Seattle, Washington
Dec 2005	**Proteomic Affinity/Capture Methods Workshop**

Recent Progress in Cancer Proteomics

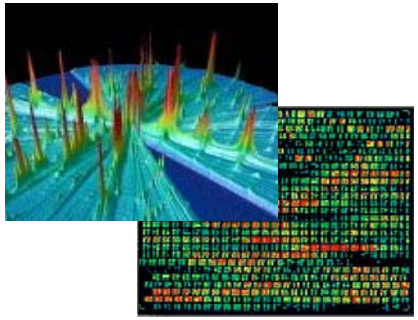
CLINICAL PROTEOMIC TECHNOLOGIES FOR CANCER

Progress in Structural Proteomics



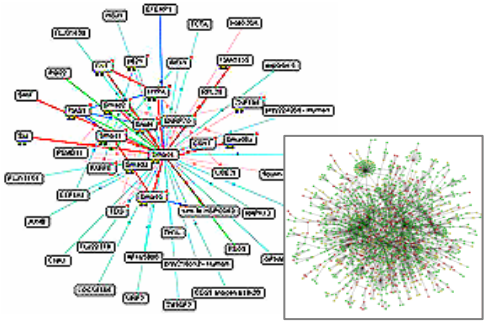
- 3 dimension structure map
- Structure – sequence relationships
- Some defined molecular targets
- Examples of target validation

Needs in Clinical Proteomics



- Quantitative measurements of proteins on basis of m/z and affinity
- Biomarker discovery
- Molecular probes
- Correlates of genotype and phenotype
- Clinical diagnostic/ theranostic platforms

Progress in Functional Proteomics



- Protein – protein interactions
- Post translation modification
- Transport mechanisms
- Molecular pathways and networks

Major Barriers to Continued Progress

Technology Barriers:

- Inability to reproduce experimental data
- Enormous diversity, range, and dynamic nature of proteins to be measured
- Limited interoperability across instruments and platforms
- Difficulty in measuring large number of features simultaneously
- Insufficient tools for data capture, analysis, and knowledge creation

Systems Barriers:

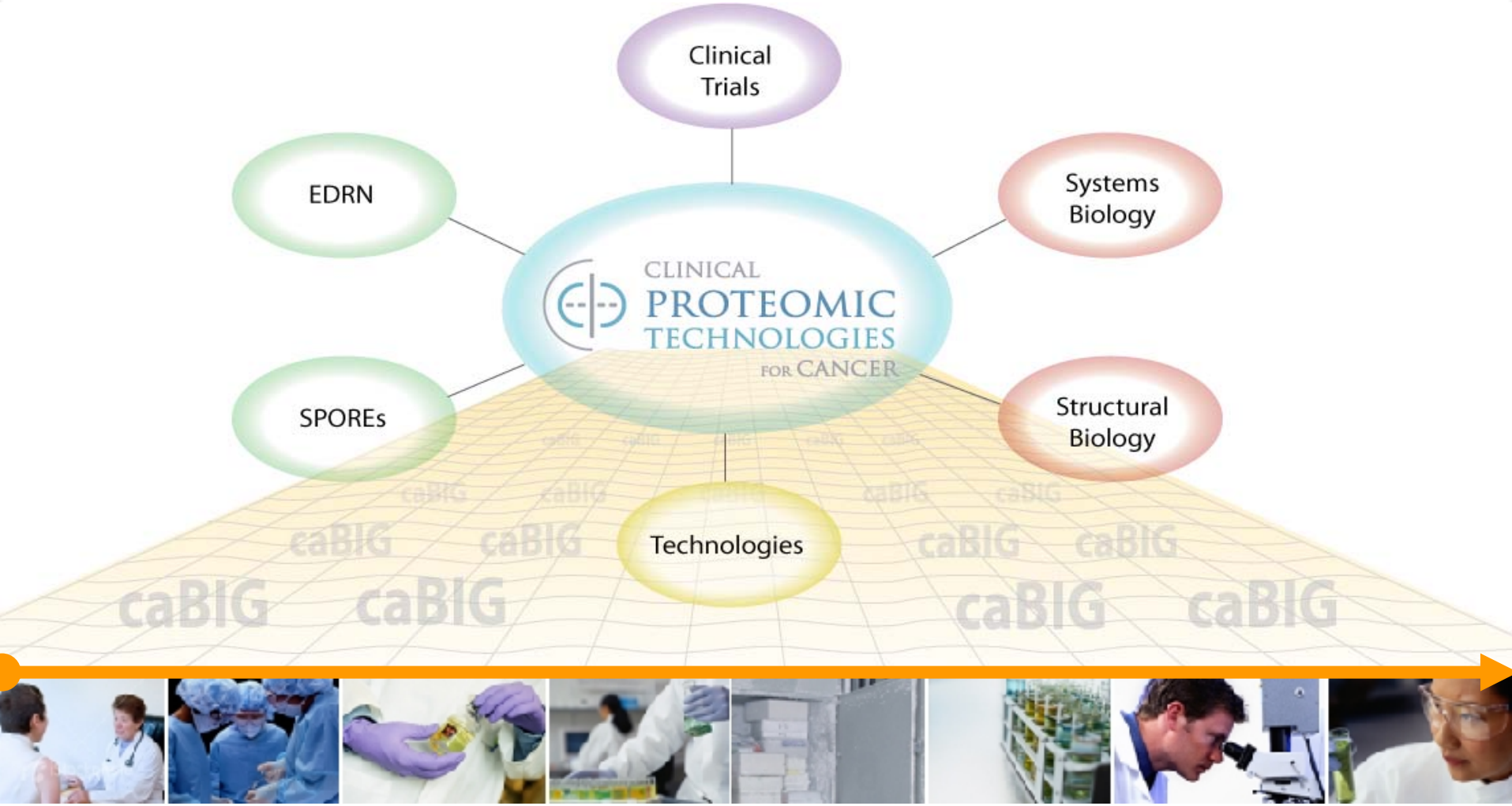
- Insufficient high-quality reagents
- Inadequate supply of biospecimens and clinical data
- Lack of standards and protocols
- No coordinated system for cancer proteomic technology, reagent, and bioinformatics development

Clinical Proteomic Technologies Initiative for Cancer

- **5-year, $104M initiative**
- **Build a foundation of technologies; data; reagents and standards; analysis systems; and infrastructure**
- **Systematically advance understanding of protein biology in cancer**
- **Accelerate discovery research and clinical applications**

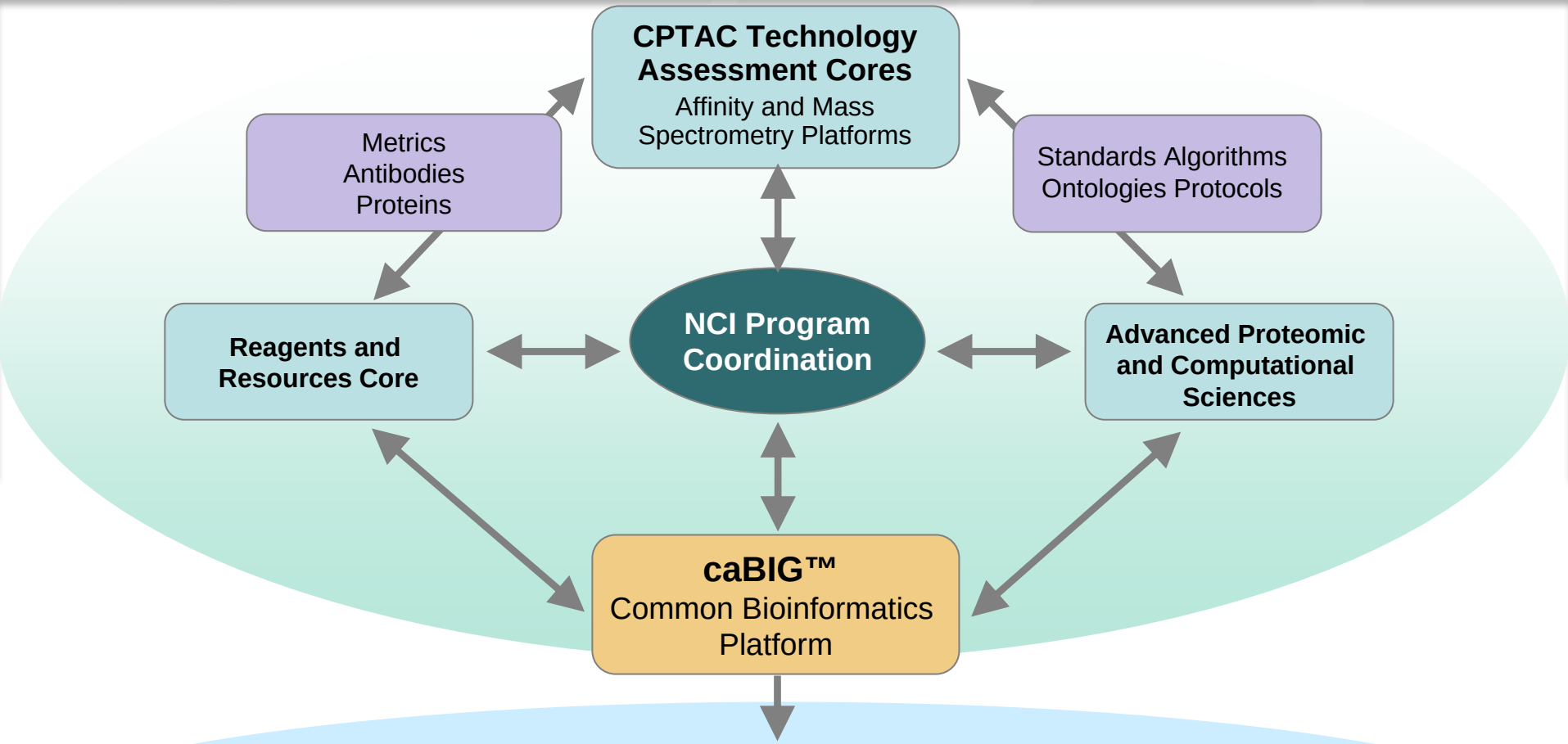
proteomics.cancer.gov

NCI Programmatic Integration



Biospecimens

Clinical Proteomic Technologies Initiative Strategy



Community Resources:

- Integrated Searchable Proteomic Database
- Highly Qualified Biospecimens
- Standardized Reagents
- Optimized Technology Platforms
- Proteomic Standards
- New Technologies

Proteomic Technologies to Facilitate Biomarker Discovery

CLINICAL PROTEOMIC TECHNOLOGIES FOR CANCER

Sites of Proteomics Technology Development

Mouse Models

Biospecimen Collection

Peptide/Protein Sample Preparation

Resource Pipeline

Data Pipeline

Lab #1 Affinity Methods

Cross Validation

Lab #2 Mass Spec

Cross Validation

Lab #3 Mass Spec

Common Resources

- Peptides and Proteins
- Antibody/Affinity Reagents
- Antibody Characterization
- Repositories
- Distribution

caBIG™

- Data Management
- Common Data Elements
- Data Standardization
- Ontology
- Vocabulary

NCI Clinical Proteomics Initiative

CLINICAL PROTEOMIC TECHNOLOGIES FOR CANCER

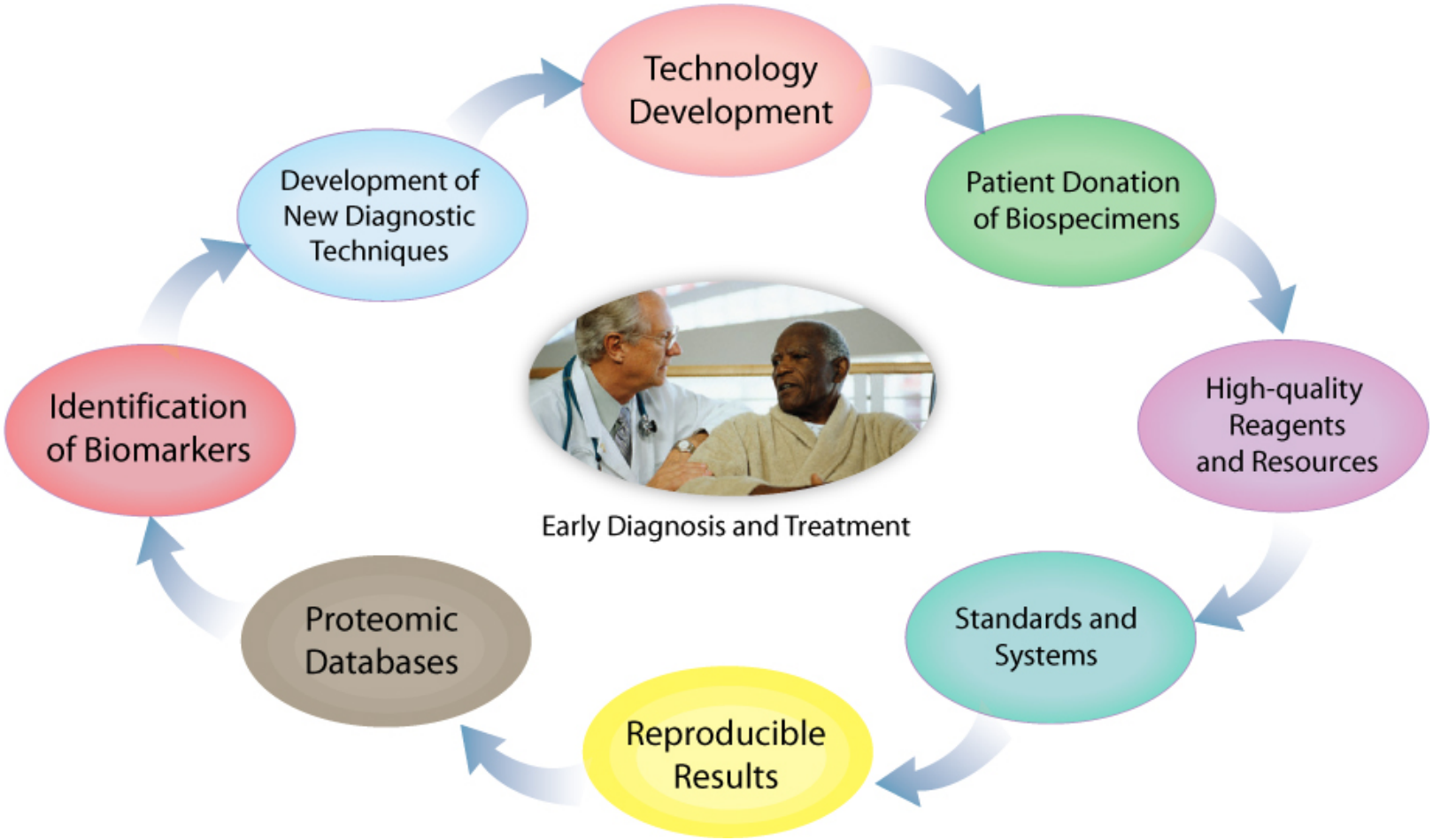
Broad consortia to standardize samples, proteomics technologies and develop protocols using common and specific models

- Multidisciplinary teams
- Coordinated and virtually integrated
- Real-time data exchange – broad access – reproducibility
- Large numbers of standardized antibodies

Standards development

- High-throughput capabilities
- Funds to drive proteomics technology development
- Common data capture, analysis, and interrogation platforms

Clinical Proteomic Technologies Initiative : Future Outcomes



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Advanced Technologies and Strategic Partnerships

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