Status Report:
The Cancer Genome Atlas Pilot Project

National Cancer Advisory Board Meeting
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Pilot Project Mission and Goal

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Mission

The Cancer Genome Atlas Pilot Project is designed to test the feasibility of a full-scale effort to systematically explore the entire spectrum of genomic changes involved in human cancer to have ***meaningful clinical impact*** in a few rationally-selected cancer types.

Goal

The overarching goal of the Pilot Project is to systematically further develop and apply current genomic analysis technologies for the expressed purpose of identifying genes and regions of potential importance to cancer – and tie this capability to the NHGRI's existing genome sequencing infrastructure for the re-sequencing of these candidates.

Enabling Factors

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Approaches/Factors

1. Human Genome Project
2. Gene families and pathways
3. Robust genomic analysis technologies
4. Sanger experience - sequenced known genes (e.g., kinases are druggable)
5. Number of early indications that somatic mutations are important potential targets

Overall Impact

1. Known human reference
2. Kinases, phosphatases, transcription factors, hormone responsiveness
3. Copy number changes, expression profiling, epigenomic technologies
4. Survey of known genes that are abnormal *prior to sequencing - BRAF*
5. *BCR-ABL, EGFR1, ERBB2*

TCGA Work Flow

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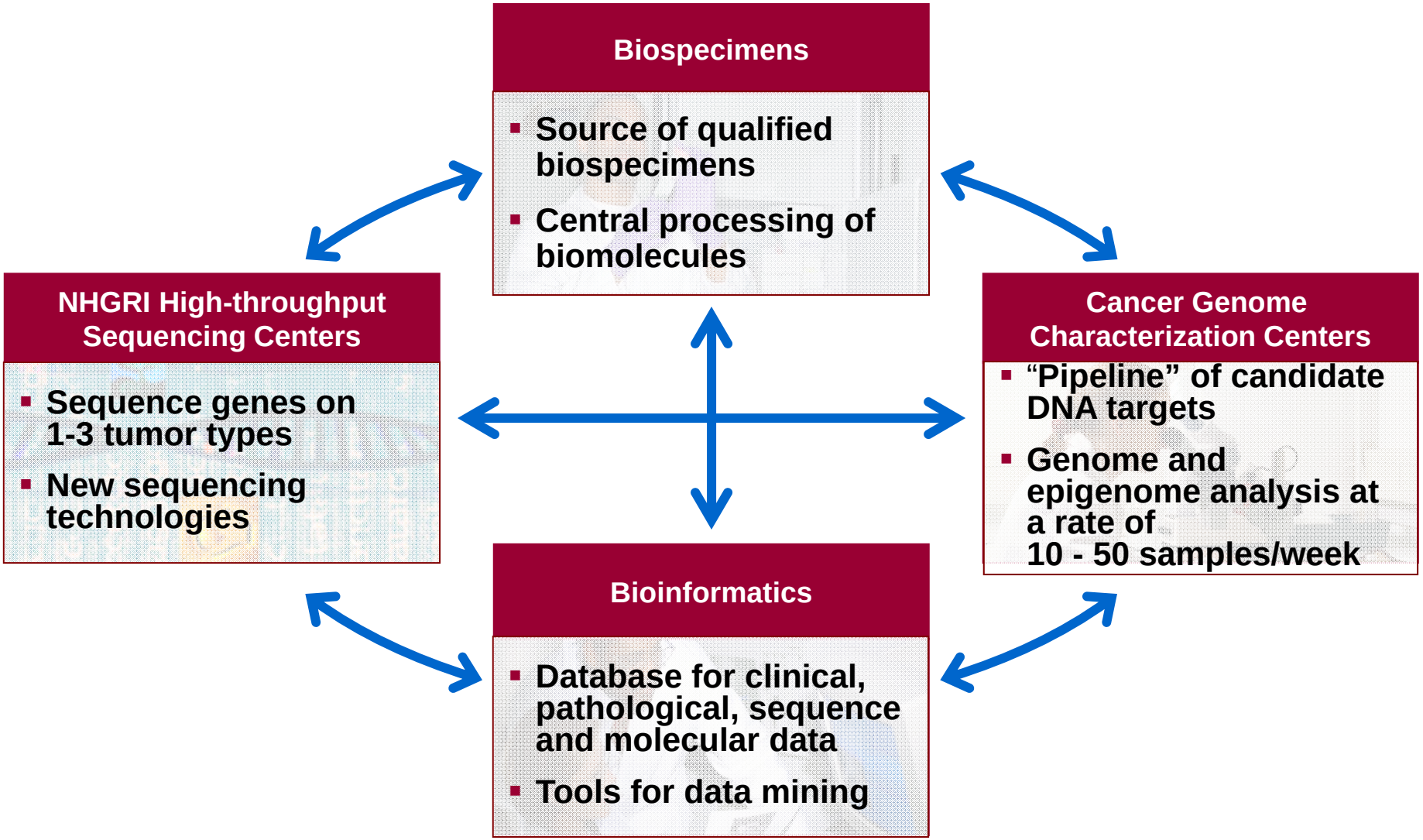

Project Development History

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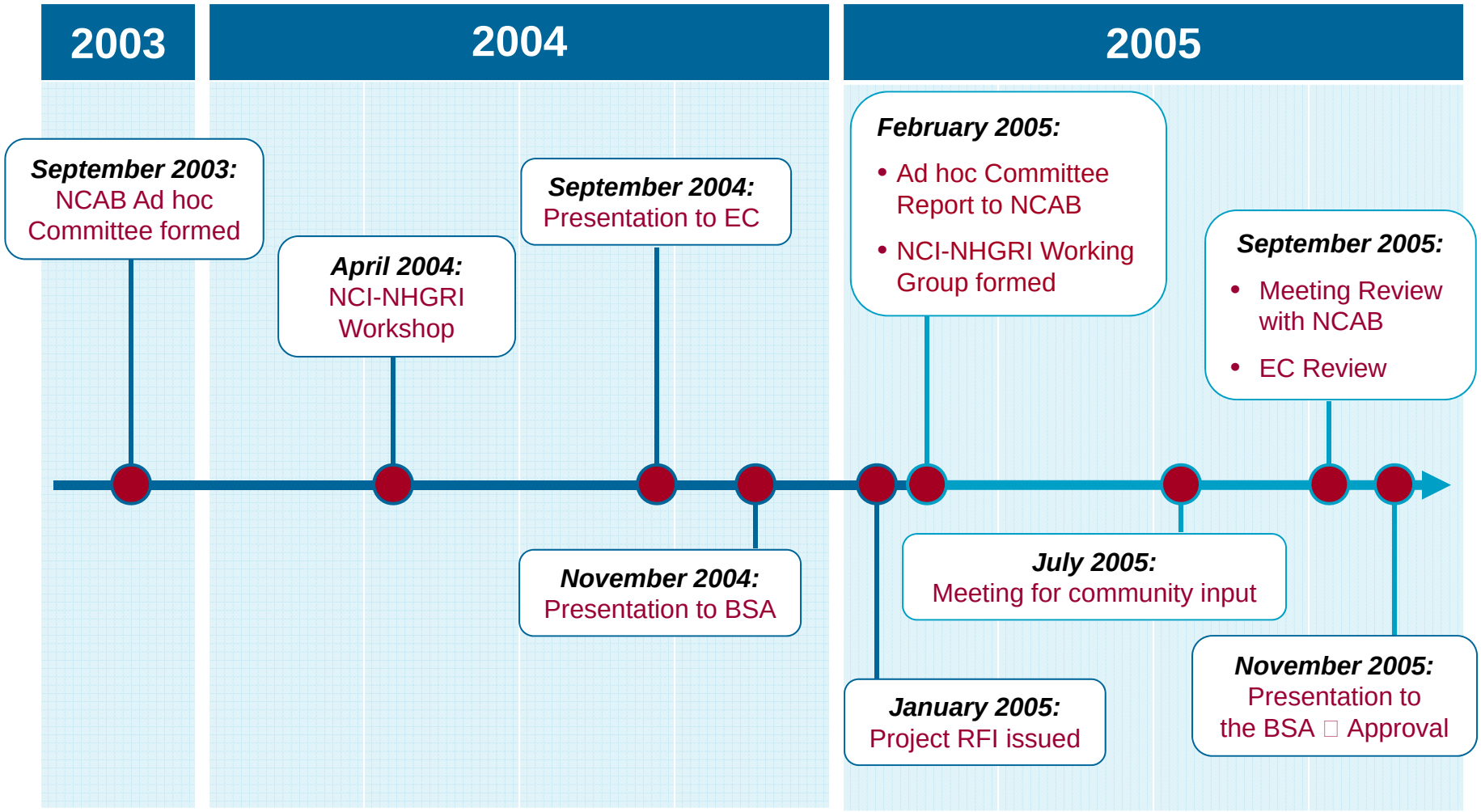

Tumor Selection for TCGA

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Criteria for tumor selection to meet TCGA Pilot Project needs and goals:

- Technical requirements
- Ethical, legal, policy requirements
- Practical requirements
- Temporal requirements

Ideal Retrospective Tumor Collections

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1. Tumor samples consist of at least 500 mg of tissue from previously untreated tumor
2. Tumor samples are frozen in OCT (glycerol-based medium)
3. At least 500 individual samples from unique cancer cases are available
4. Samples are properly consented for use in this project
   - ✓ Current consent is sufficient or
   - ✓ Patients may (and can) be re-consented in a timely fashion
   - ✓ Consent is “all or none”; not tiered
5. All tumors have matched normal samples (e.g. this should be white blood cells from 5-10 ml of normal blood and normal tissue from the same organ as the primary tumor)
6. Samples represent a single histopathologic type of tumor and/or (if a solid tumor) derived from a single cancer site (e.g., brain, breast, lung, etc)
7. Individual tumor samples contain at least 80% tumor cells
8. The tumor samples are derived from patients entered in a clinical trial with:
   - ✓ Uniform entry criteria
   - ✓ Consistent treatment (The patients may be treated on different arms of a randomized study)
   - ✓ Clinical Data that has undergone regular audits within the parameters of the ongoing trial
9. Tumors are from a primary tumor site (i.e. not regional or distant metastases)

Human Cancer Biospecimen Core Resource

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- Verify authenticity and perform the pathologic QC of qualified tumors from existing collections
- Perform central processing of specimens
- Develop and monitor the SOPs for prospective specimen collection
- Track all specimen-related operations (consent, acquisition, transport, processing, QC, distribution) through caBIG
- Provide “standard” samples for technology platform comparisons
- Distribute materials

Cancer Genome Characterization Centers (CGCCs)

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- **Genome characterization**
  - ✓ **Expression profiling**
  - ✓ **Copy number changes**
  - ✓ **Epigenomics**
- **Improve existing technologies**
  - ✓ **Epigenomics to meet required throughput rate**
  - ✓ **Copy number detection and expression profiling for characterizing small amount of biological samples**
- **Real-time data release into public database**
- **CGCCs RFA:**
  - ✓ **Mechanism: U54 (cooperative agreement)**
  - ✓ **$11.7 million – year 1**

Genome Sequencing Centers

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- **High-throughput Genome Sequencing Centers (NHGRI)**
  - ✓ **Sequence large number of targets from at least 2 tumor types**
  - ✓ **Develop and integrate sequencing technologies**

- **Genome Sequencing Centers RFA:**
  - ✓ **Mechanism: U54 (cooperative agreement)**
  - ✓ **$50 million in sequencing for TCGA**

Bioinformatics Core

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- caBIG platform and standards
- Data management
- Database(s) development
- Specific Analytic tools
- caBIG standards participation
- Inter-program communication

Technology Development

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- **Opportunities For Technology Development**
  - ✓ Genomic rearrangement, epigenetic assays
  - ✓ Highly parallel single molecule assays
  - ✓ Method for selecting / enriching defined regions of genome
  - ✓ Magnitude improvement in cost, throughput, accuracy, and precision

- **Technology Development RFA:**
  - ✓ Mechanisms: SBIR/STTR; R21 (exploratory/development)
  - ✓ Investment $2 million SBIR/STTR year 1

The Cancer Genome Atlas Pilot Project

- Public Launch: December 13, 2005 at news conference and advocates meeting
- Partnership between NCI and NHGRI
- Three-year, $100 million pilot project

http://cancergenome.nih.gov

Broad Media Response

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Result: Positive scientific, business, and national consumer coverage

CNN

Unraveling cancer

Marketplace®

NIH launches project to map cancer genome

BioIT World

TCGA – The Cancer Genome Atlas Pilot Launched

PBS

Unlocking cancer genes

Factors to Assess the Pilot

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- Robust genomic analysis of two tumors – identification of significant number of candidate genes for re-sequencing
- Genome characterization and analysis performed with sufficient power (>500 samples/tumor) to provide a “pipeline” for re-sequencing important (occur at >5-10% frequency) cancer genes/regions
- Ability to find genomic changes (e.g. loss of heterozygosity, deletions, amplifications, translocation, and epigenetic modifications) and re-sequence selected of these aberrations
- Ability to differentiate tumor subtypes based on genomic alterations
- Establishment of a public database of sequences, characterization results, and clinical data
- A stretch – but many believe that new cancer genes could be discovered from the tumors studied – beyond the “street lamps”

Upcoming Milestones

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