



Status Report: The Cancer Genome Atlas Pilot Project

National Cancer Advisory Board Meeting
September 6, 2006

Anna D. Barker, Ph.D.
Deputy Director, National Cancer Institute



TCGA: An NCI – NHGRI Collaboration in Medical Genomics



The Cancer Genome Atlas (TCGA)
is a 3-year pilot project of the
National Cancer Institute and
the National Human Genome Research Institute
to increase our comprehensive understanding of the
genetic basis of cancer

- It is anticipated that TCGA's integrated database of molecular and clinical information will provide scientists unprecedented opportunities to discover and develop a new generation of targeted diagnostics, therapies and preventives for cancer -

Enabling Rationale for TCGA

THE CANCER GENOME ATLAS



Achievements

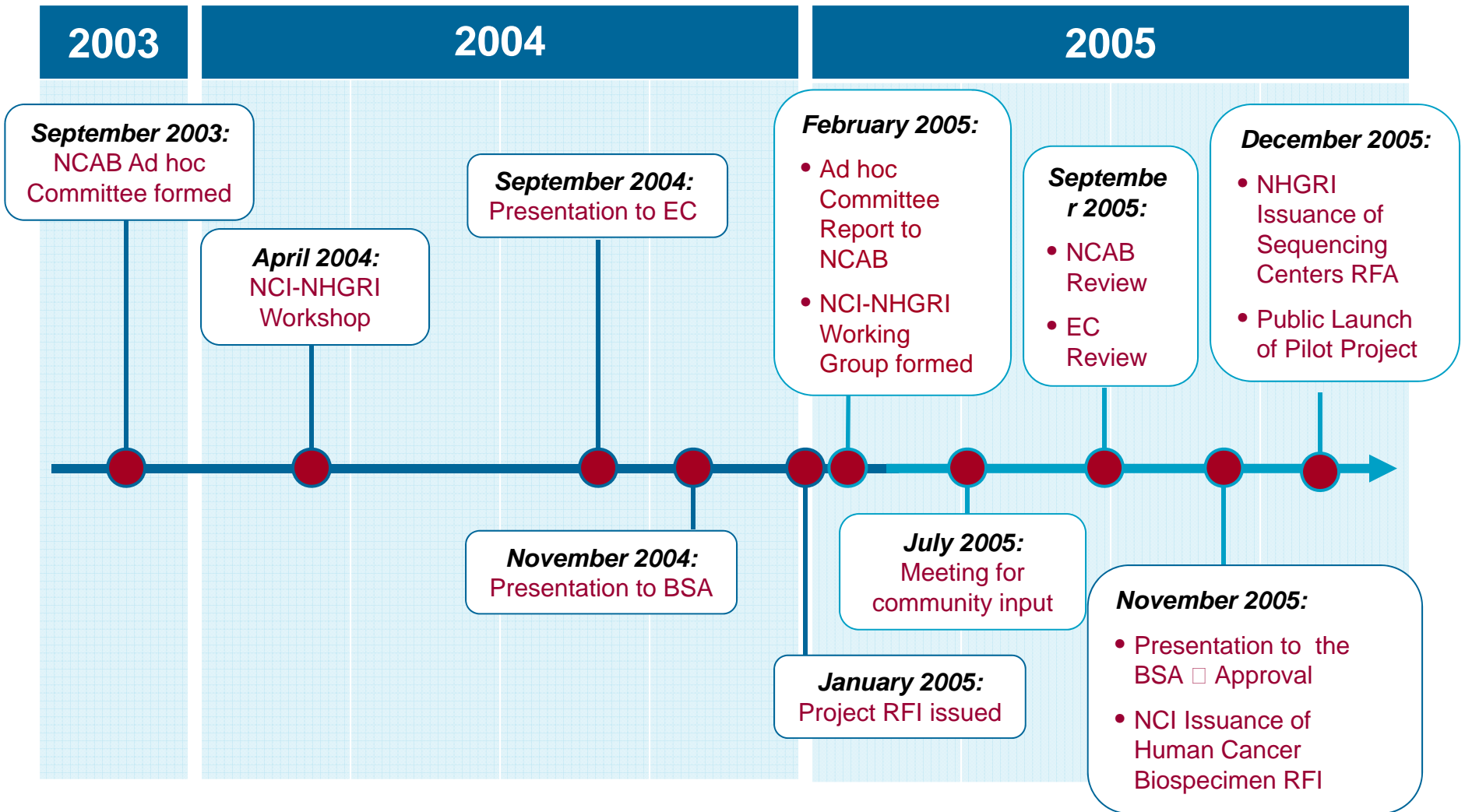
1. Human Genome Project
2. Gene families and pathways
3. Robust genomic analysis technologies
4. Sanger experience - sequenced known genes (e.g., kinases are druggable)
5. Number of early indications that somatic mutations are important potential targets

Overall Impact

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

TCGA Development Milestones

THE CANCER GENOME ATLAS



Project Development Milestones

THE CANCER GENOME ATLAS



2006

February 2006:

- NCI Issuance of Biospecimen Core Resource RFP

March 2006:

- NCI Issuance of Cancer Genome Characterization Centers RFA

May 2006:

- Data Release Workshop

July/August 2006:

- Site visits to Biorepositories

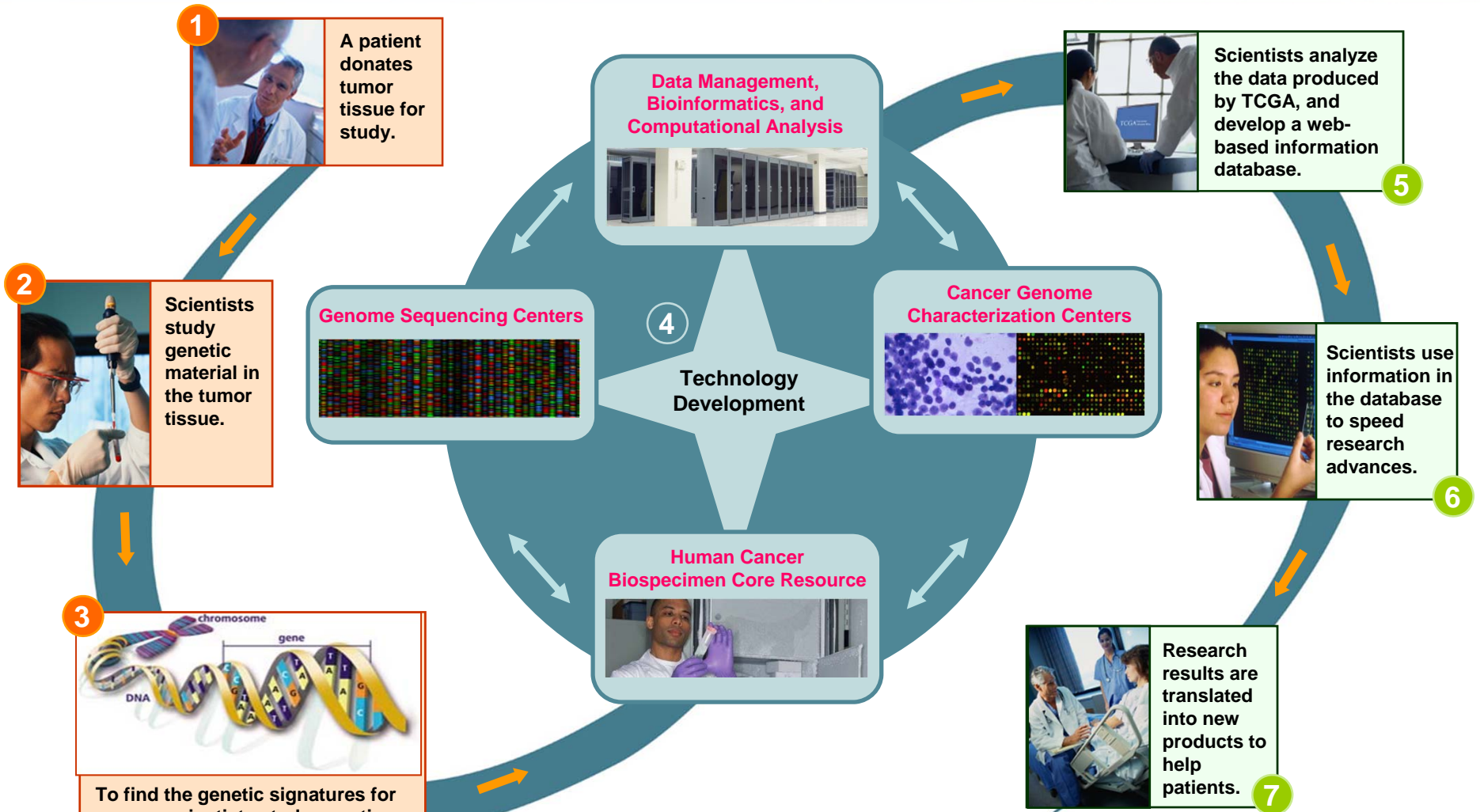
September/October 2006:

- Selection of tumor types
- NCI Funding of Biospecimen Core Resource
- NCI Funding of Cancer Genome Characterization Centers

December 2006:

- NHGRI Funding of High-throughput Sequencing Centers

The Various Components of TCGA – Procurement Processes Ongoing



■ Patient Community

■ TCGA Network

■ Research & Medical Communities

Upcoming Milestones for TCGA

THE CANCER GENOME ATLAS



- Finalize selection and award the Biospecimen Core Resource (Scheduled for September 13, 2006)
- Select the tumors to be used in TCGA Pilot (Single and/or multiple biospecimen collections) (Scheduled for September 13, 2006)
- Finalize selection and award the Genome Characterization Centers (October, 2006)
- Finalize selection and award bioinformatics support activities (October, 2006)
- Finalize selection and award Genome Sequencing Centers (NHGRI, December, 2006)
- Project launch – January, 2006

TCGA Biospecimen Core Resource (BCR) Functions

Central to the Success of TCGA Pilot, the BCR will:

- Verify all biologic and clinical data and perform the pathologic QC of qualified tumors from selected existing collections
- Perform central processing of specimens to provide uniform biomolecules and distribute to both genome characterization and sequencing centers
- Track and quality assure all specimen-related operations (consent, acquisition, transport, processing, QC, distribution)
- Provide “standard” samples for technology platform comparisons
- Develop (with the Office of Biorepositories and Biospecimens Research) and monitor the SOPs for prospective specimen collection
- Serve as a member of TCGA’s Steering Committee

(Selected organization to support BCR will be named in Mid-September)

Categories of Biospecimen Collections (Tumor Types) for TCGA

To initiate TCGA one tumor type will be selected from qualifying biorepositories in three categories: a tumor representing a major public health impact; a second tumor type that demonstrates a high degree of homogeneity; and the third, a tumor collection that derives from a completed clinical trial

Biospecimen Selection Process:

Evaluation Process

- **2005 - A request for information (RFI) and notification to cancer centers**
- **Biorepositories identified from RFI that met rigorous criteria (quality of samples, pathology, clinical and biologic data) and achieved ethical and legal specification were then screened using a series of primary criteria**
- **Qualifying collections were further evaluated using secondary criteria – and biorepositories were site-visited**
- **Factors such as timing, logistics of collections and informed consent were factored in at this stage and a ranking in the three categories was developed**
- **Qualifying biorepositories were further reviewed with input from an expert technical panel – composed of representatives from the surgery, pathology, scientist, patient advocate and bio-ethicist communities**

Biospecimen Collections Selection Criteria

THE CANCER GENOME ATLAS



Primary Criteria (Must meet all primary qualification criteria)

- At least 250 samples of the same cancer type (combining samples from same cancer type may be pursued to insure statistical validity)
- Each cancer sample must be accompanied by samples of matched “normal” tissue, such as blood, from the same patient
- Must be from clinical trial or similar study
- A minimum of 0.2 grams of tissue
- Patients gave permission to be re-consented

Secondary Criteria (Collections that met primary criteria were ranked for the following)

- Quality-control analyses of tissue sample and biomolecules
- Sample characteristics
- Sample collection procedures and storage
- Clinical trial protocol and donor enrollment
- Informed consent
- Clinical data quality
- Clinical data electronic status
- Institution’s contractual capabilities

Telephone Interviews were followed up with site visits by an NCI-NHGRI team

Cancer Genome Characterization Centers (CGCCs)

THE CANCER GENOME ATLAS



- **Technology platforms for high throughput genome characterization**
 - ✓ Expression profiling
 - ✓ Copy number changes
 - ✓ DNA methylation (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:**
 - U24 (cooperative agreement)
 - \$11.7 million
 - Peer Review: August 8-9, 2006
 - Awards to be announced: October 2006

Genome Sequencing Centers

THE CANCER GENOME ATLAS



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

- **Genome Sequencing Centers RFA:**
 - ✓ Mechanism: U54 (cooperative agreement)
 - ✓ \$50 million in sequencing for TCGA
 - ✓ Peer Review: July 13, 2006
 - ✓ Awards to be announced: December 2006



caBIG Will Provide a Bioinformatics Platform for TCGA

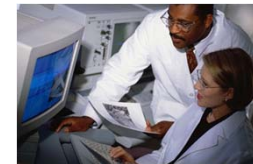
THE CANCER GENOME ATLAS



Molecular Data

Clinical Data

Data from Genome Characterization and Sequencing Centers



NCI's Cancer Bioinformatics Grid (caBIG): Principal Bioinformatics Resource for the Development of a Public TCGA Database

Ethical, Legal, and Policy Considerations

THE CANCER GENOME ATLAS



TCGA (and other large scale medical genomics efforts) must address several ethical, legal, and policy issues/questions:

- How detailed should informed consent be – more information vs. less?
- Who should have access to data?
- How do we leverage and capitalize on potential for progress against disease and ensure privacy protection?
- Will we need new forums of patients, clinicians, researchers, ethicists to discuss these issues and inform policy?

Ethical, Legal, and Policy Considerations (continued)

THE CANCER GENOME ATLAS



Informed Consent Issues

- **Permission for detailed genomic research**
- **Permission for broad future research use of samples and health information**
- **Permission to place genomic & health information in widely-accessible databases**
- **Risks associated with loss of privacy**
- **Potential benefits for future cancer patients**
- **Problems related to withdrawal**

Some Expectations for TCGA - The Pilot Project

THE CANCER GENOME ATLAS



Three-Year Horizon

- Completion of genomic analysis of three tumors
- Ability to identify specific alterations in genes associated with cancer
- Ability to differentiate tumor subtypes based on genomic alterations
- Establishment of a database with all data from TCGA Pilot Project that scientists can access for follow-up experiments

TCGA's Long View

THE CANCER GENOME ATLAS



- Identification of somatic changes in cancer genomes that could establish the molecular basis for each cancer – and inform and enable a new era of molecular oncology
- A molecular taxonomy of cancer
- New molecular targets for diagnostics, therapeutics and preventives
- Improved ability to stratify patients for clinical trials



For More Information: Joint NCI-NHGRI TCGA Website

THE CANCER GENOME ATLAS



- **Updates on TCGA website:**
 - ✓ Information for patients, scientists, clinicians, policymakers, and the public
- **Coming Soon:** Sign up at the TCGA website to receive automatic updates and event news

The screenshot shows the homepage of the TCGA website. At the top, there are logos for the National Cancer Institute and the National Human Genome Research Institute. The main header reads "THE CANCER GENOME ATLAS" with a search bar and a "GO" button. Below the header is a navigation menu with links for "About TCGA", "Funding", "Program Components", "Media Center", and "Related Initiatives". The main content area features a large banner image of a DNA double helix and scientists working in a lab. Below the banner, there are three main sections: "Mission and Goal", "Message from the Institute Directors", and "TCGA Pilot Project Launched". Each section includes a brief description and a "Learn more" link. On the right side, there are two smaller featured articles: "TCGA: How Will It Work?" and another "TCGA Pilot Project Launched" article, both with "Click here" links. At the bottom, there is a footer with navigation links (Home, Text-Only Version, Contact Us, Policies, Accessibility, Search, Site Map) and logos for the National Cancer Institute, National Human Genome Research Institute, and FIRSTGOV.

<http://cancergenome.nih.gov>

The Future: Personalized Cancer Medicine

THE CANCER GENOME ATLAS

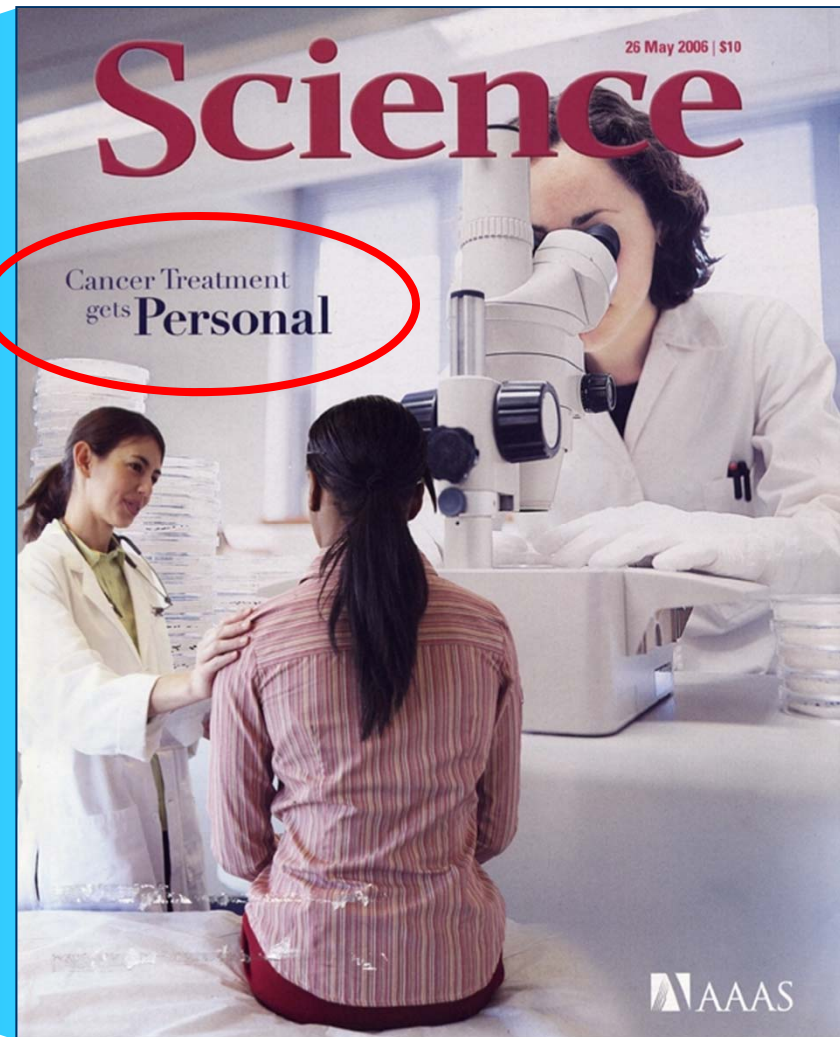
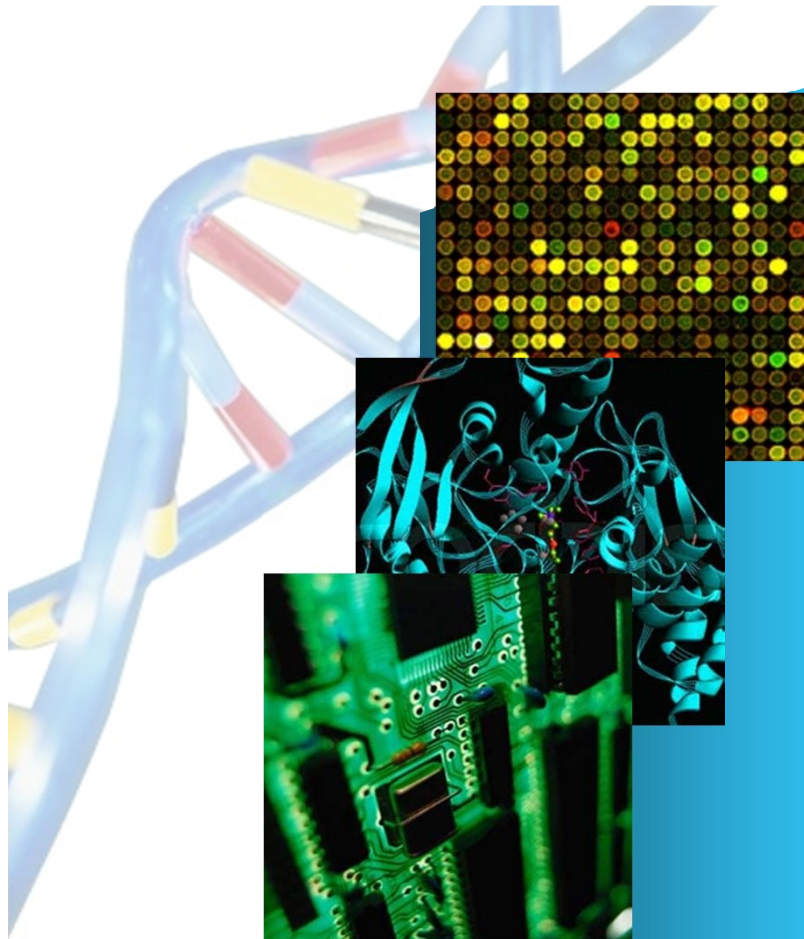


Image courtesy of *Science*, May 26, 2006