Update on The Cancer Genome Atlas for the National Cancer Advisory Board

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on behalf of the TCGA Project Team

September 7, 2010

The TCGA Project Team

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- **NCI**
  - Ann Barker
  - Joe Vockley
  - Kenna Shaw
  - Laura Dillon
  - Greg Eley
  - Carl Schaeffer
  - Martin Ferguson
  - Peter Fielding
- **NHGRI**
  - Brad Ozenberger
  - Jacqueline Palchik
  - Jane Peterson
  - Peter Good
  - Elizabeth Thomson
  - Julia Zhang

The Directors: Harold Varmus, Eric Green, Francis Collins

Outline

- Review the last presentation to NCAB (Sept 2009)
- Summarize overall organization of TCGA and the tumors being targeted (plus the ICGC targets)
- Update on status of sample accrual and sequencing
- Future sample accrual goals
- Challenges
- Approaches to challenges

Background

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- **TCGA was initiated as a pilot designed to explore the processes needed to perform high-throughput, large scale disease-focused genome characterization, data integration and analysis**
  - **Biospecimens**
  - **Large-scale genome characterization and sequencing**
  - **Integration of data, laboratories and teams**
  - **Policies (e.g. data standards, data access, informed consent**

TCGA Pilot Program Conclusions

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- This comprehensive approach can produce clinically relevant data
- **At the level of individual genes, cancer genomics is complex. At the level of pathways, more coherence can be observed.**

TCGA Phase II: Overview

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- **During the two years of ARRA funding – plan to complete comprehensive genome characterization of 10 tumor types (at 200 cases/tumor type as a discovery set and more depending on tumor type; 180 exomes; 20 whole genomes/tumor), and partial characterization of 10 more (at 100 cases/tumor type)**
  - **GCCs will perform expression, copy number, methylation and miRNA characterization**
  - **Genome Sequencing Centers will use Nex-Gen sequencing technologies – exomes and whole genomes (cost dependent)**

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  - Genome Sequencing Centers will use Nex-Gen sequencing technologies – exomes and whole genomes (cost dependent)
- **Genome Data Analysis Centers will integrate data from GCCs – GDAC-Bs will further integrate data, create new models and tools to refine and further add value to data for communities**

TCGA Project Pipeline

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Supplementary Figure 1

Pathology QC

DNA & RNA Isolation, QC

Analysis

Sequencing

Expression, CNA & LOH, Epigenetics

Analysis

Data and Results Storage & QC

GDAC

Integrative Analysis

Comprehensive **Knowledge** of a Cancer Genome

= Process

= Data

= Results

= BCR = GSCs = CGCCs = DCC = GDACs

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Supplementary Figure 1

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TCGA Tumor Projects

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Projects with comprehensive data available

- **Glioblastoma†**
- **Ovarian**

Projects in progress (partial data sets available)

- **Acute Myeloid Leukemia**
- **Colon Adenocarcinoma**
- **Rectal Carcinoma**
- **Lung Adenocarcinoma**
- **Lung Squamous Cell Carcinoma**
- **Renal Clear Cell Carcinoma**

TCGA Tumor Projects

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Projects recently begun or upcoming

- Breast (multiple types)*
- Bladder
- Cervical
- Head and neck
- Liver
- Lymphoma
- Melanoma
- Multiple myeloma
- Pancreatic
- Prostate
- Sarcoma
- Stomach*
- Thyroid
- Uterine* (endometrial)

ICGC Projects (June, 2010)

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- USA
  - TCGA projects
- Canada
  - pancreatic*
  - prostate
- Australia
  - pancreatic*
  - ovarian
- China
  - stomach
- EU/France
  - renal carcinomas
- EU/United Kingdom
  - breast cancers*
- France
  - breast cancers*
  - hepatic (alcohol-associated)
- Germany
  - pediatric brain cancers
- India
  - oral
- Italy
  - rare pancreatic types
- Japan
  - hepatic (virus-associated)
- Spain
  - chronic lymphocytic leukemia
- United Kingdom
  - breast cancers*

*Collaborative

Goals for ARRA Period

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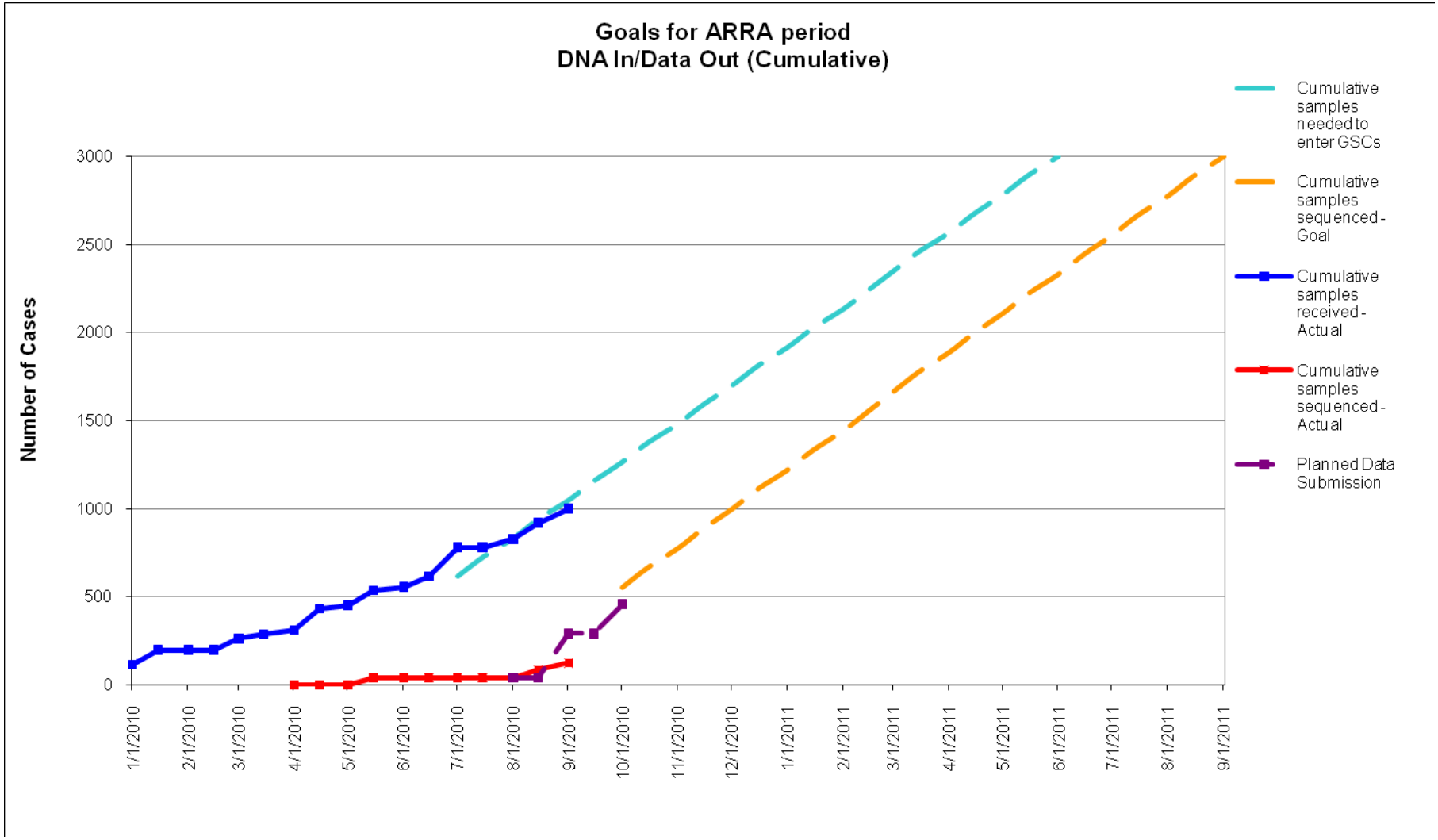

TCGA Sample Accrual
(Sept 2010)

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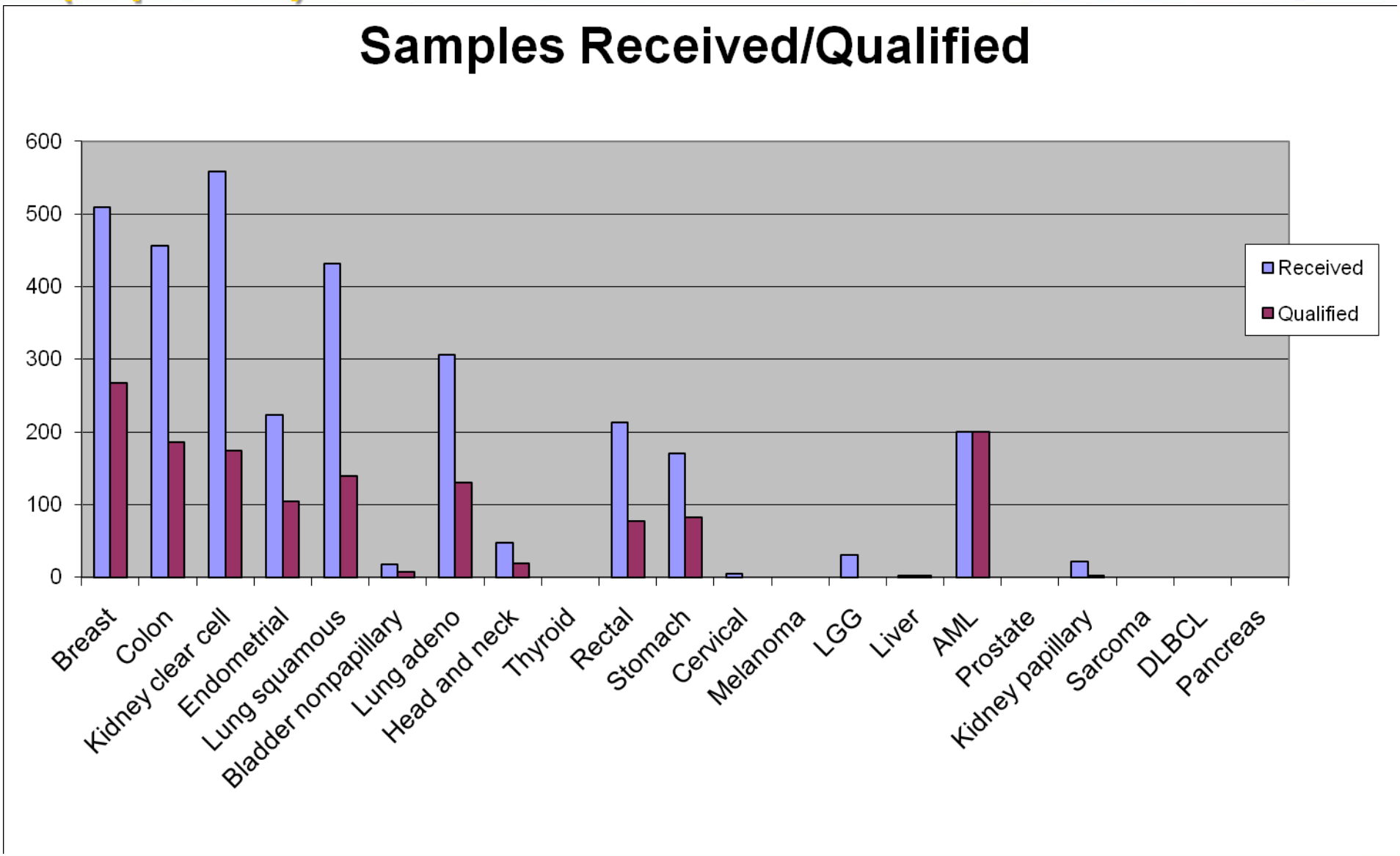

TCGA Sequence Data Submission

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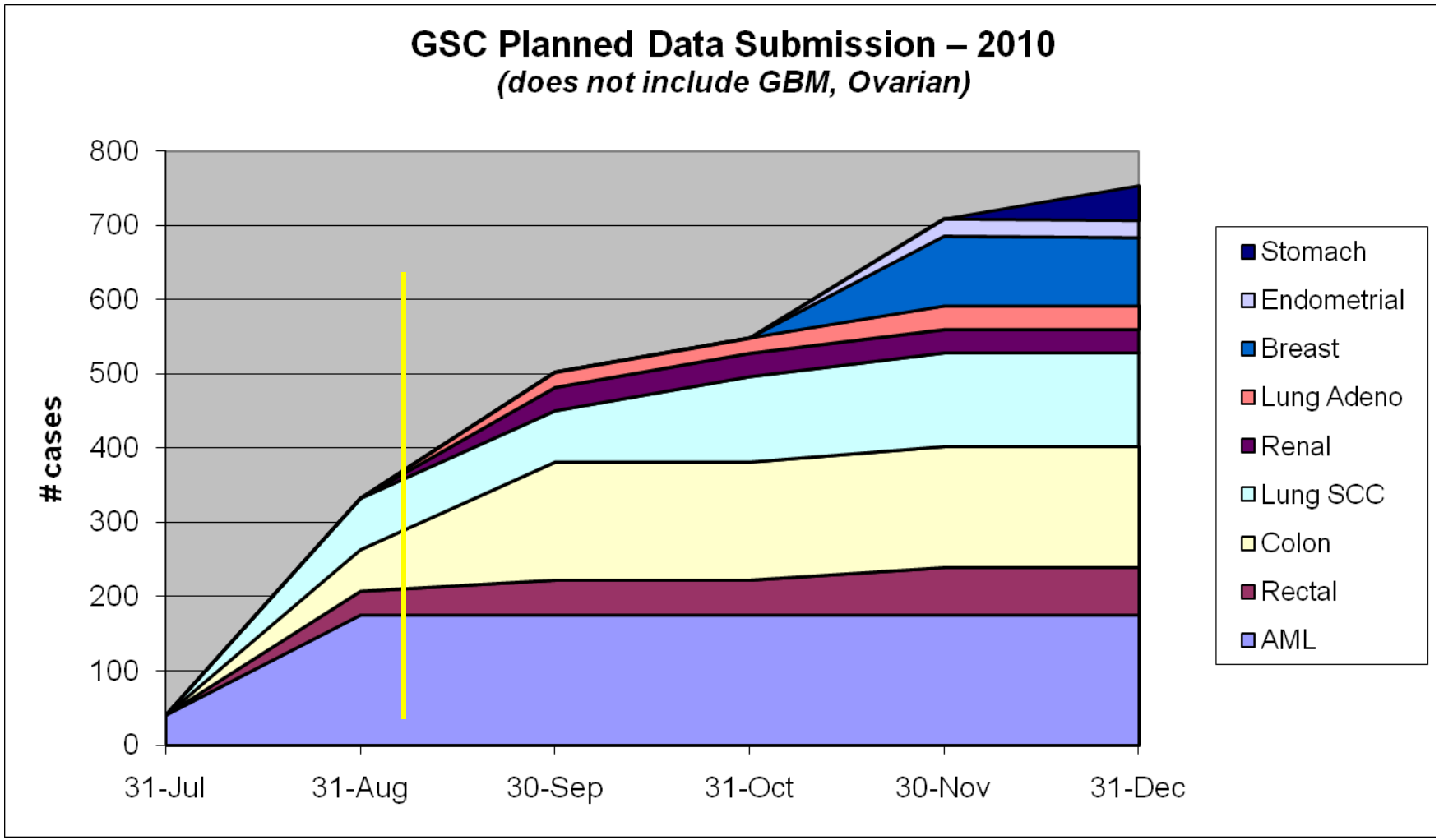

TCGA to date t

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Tumor Type	GCC assays	Whole Exomes	Whole Genomes
Ovarian	560	434 86 in progress	10 17 in progress
AML	162 39 in progress	15 135 in progress	26 29 in progress
Colon	103 41 in progress	52 51 in progress	0
Rectal	50 17 in progress	0 67 in progress	0
Breast ductal	0 233 in progress	0 186 in progress	0
Lung adeno	21 74 in progress	0 95 in progress	0
Lung scc	69 45 in progress	0 114 in progress	0
Endometrial	0 70 in progress	0 70 in progress	0
Renal	32	0 32 in progress	0
Gastric	0 82 in progress	0 82 in progress	0

http://cancergenome.nih.gov/dataportal

TCGA Sample Accrual
(through March 2011)

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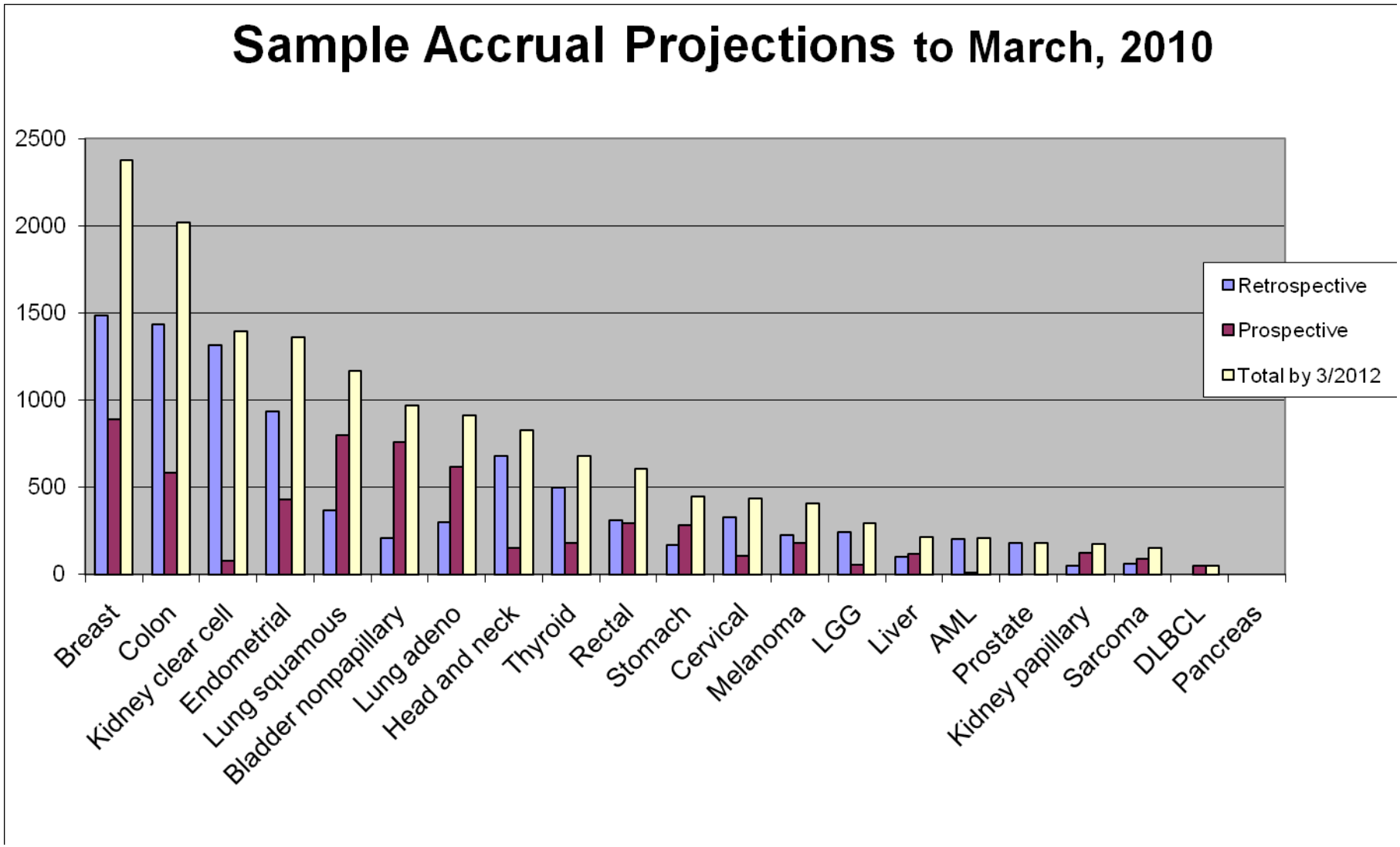

TCGA Sample Criteria (Pilot)

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- Primary tumor only
- Snap frozen
- ~ 200 mg
- No more than 20% necrosis ; ≥ 80% tumor cells
- Normal tissue: Blood (buffy coat/white cells); adjacent normal tissue or buccal cells; or ≥ 13µg high-quality DNA
- All “Tier One” Clinical Data Elements (15 or more)
- Treatment naïve

Challenges for TCGA Production

- **Sample criteria**
  - **Tumors for which pre-treatment is standard of care**
  - **Tumors of lower purity**
  - **Use of adjacent tissue as “germ line” comparison**

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- Sample criteria
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  - Tumors of lower purity
  - Use of adjacent tissue as “germ line” comparison
- **Multiple concurrent projects**
- **Project length**

Organization of TCGA Sequencing

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- ***GBM and ovarian pilot projects*** **– samples were apportioned among the 3 GSCs**

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- *AML and colon* – designated primary and secondary GSCs; 10 exomes and 1 whole genome cases to be done by both centers
  - AML – Wash U / Broad Institute
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- ***Subsequent projects* – to be assigned to a single GSC for all data generation, validation, and analysis; 10 exomes to be duplicated in a second GSC for QA**
  - **Broad Institute: lung adeno, lung squamous, gastric**
  - **Wash U: breast projects, endometrial**
  - **Baylor: rectal, kidney**