

Closing Remarks

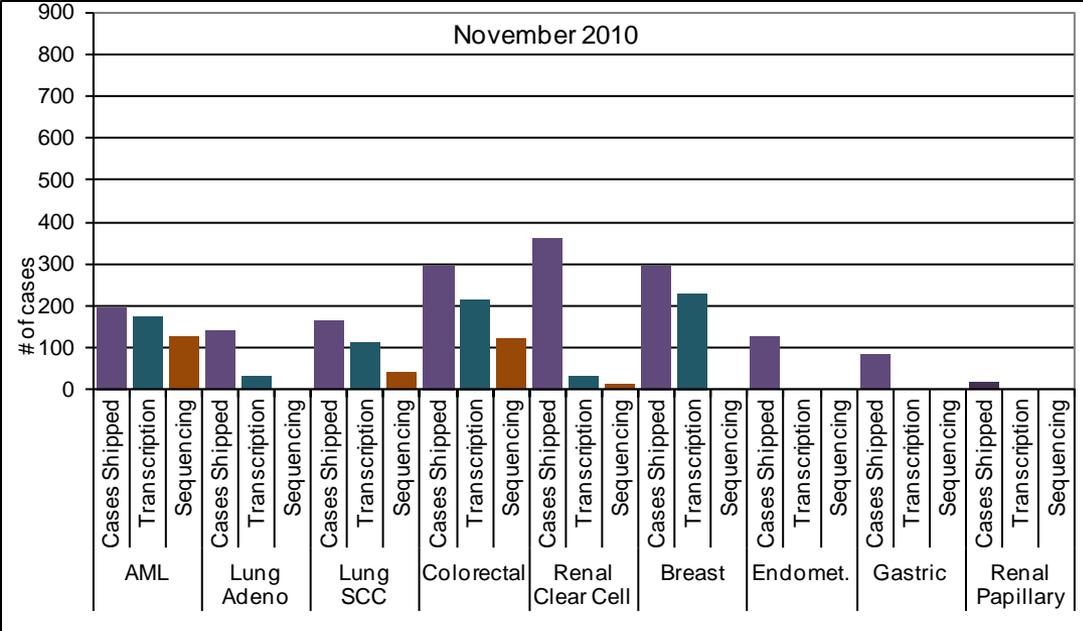
Elaine Mardis

1st Annual TCGA Scientific Symposium

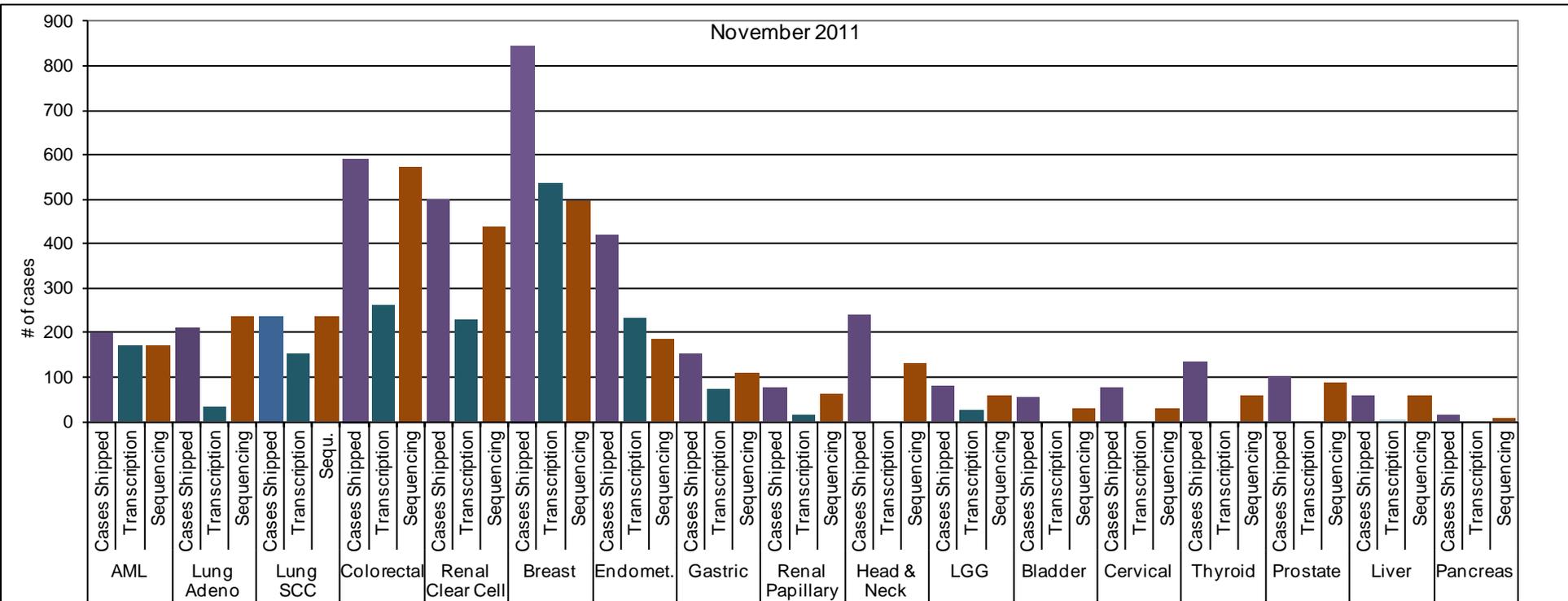
Challenges from the 2005 White Paper



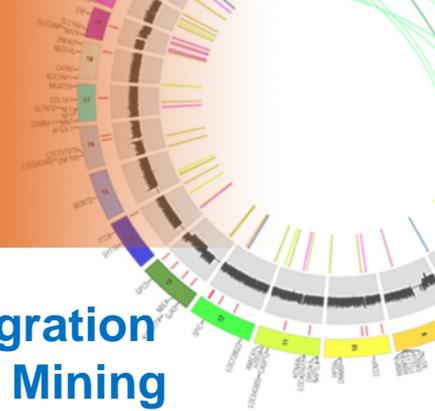
- **Overarching Goal**
 - Obtain a comprehensive description of the genetic basis of human cancer
- **Overarching Assessment of Success**
 - Short-term
 - ✓ Milestones such as samples collected, analyzed, made accessible to the community
 - Long-term
 - Impact on the lives of patients
- **Strategy**
 - Create a large collection of samples from all major types of cancer ensuring:
 - ✓ Patient consent
 - **Clinical annotation**
 - ✓ Sample quality
 - **Sample quantity**
 - ✓ Availability of matched DNA
 - **Ethnic diversity**



Nov 2010 Status
Vs.
Nov 2011 Status



TCGA Data Production Pipeline



Massive Scale of raw Sequence Data Production, Processing, and Storage



Petascale data with massive compute and storage cost

CGHub sequence data repository at San Diego Supercomputer Center (SDSC) ~5 PB BAMs for 10K tumor cases

Issues: Data-intensive computing with large-scale raw data processing, massive transfer and storage, controlled access, privacy, integration with metadata

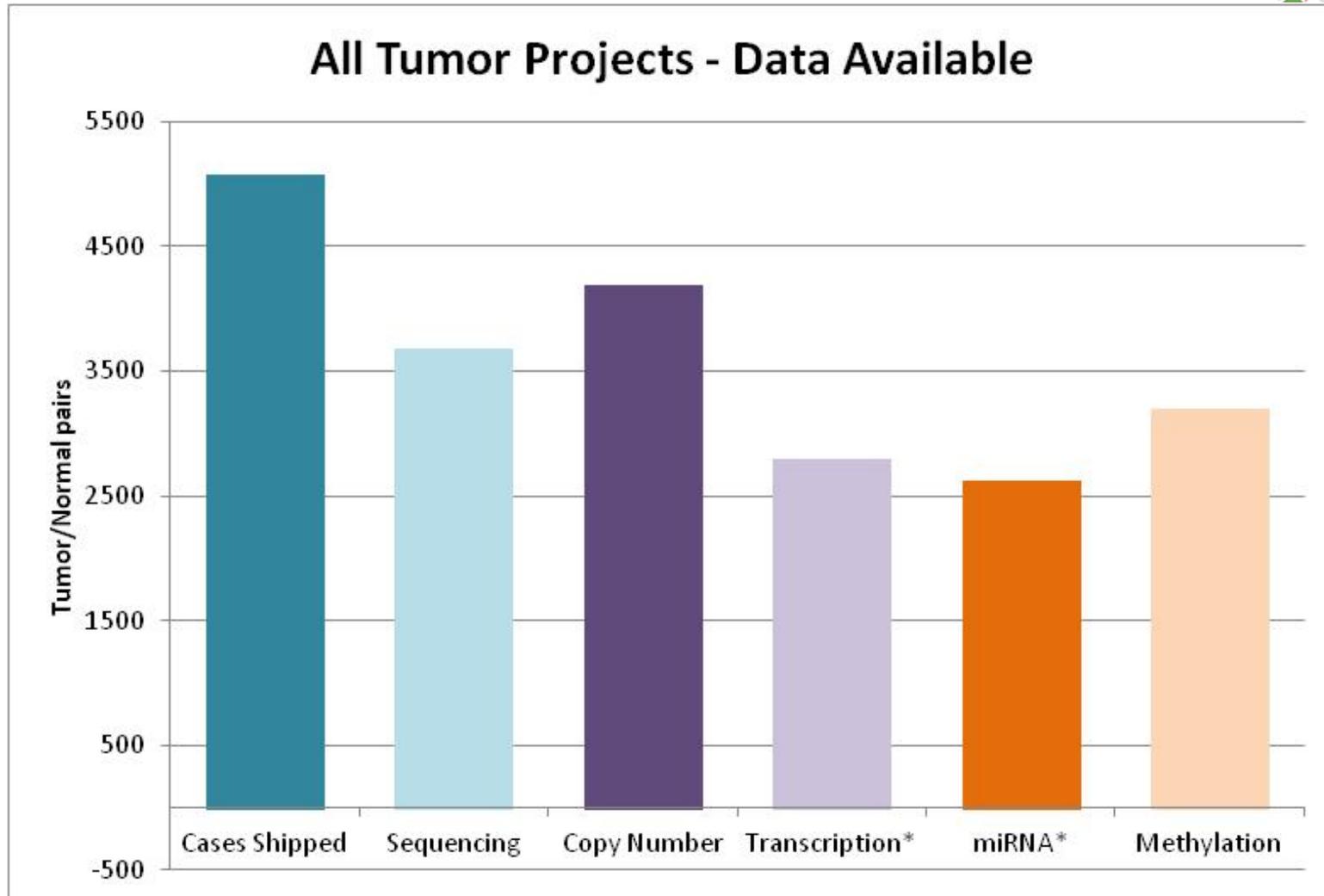
360° Integration and Data Mining

- Mutation calling
- Structural variation
- DNA vs RNAseq
- Gene expression
- Transcript
- Methylation
- Pathway analysis
- Clinical correlations

DCC data sets (Terascale)

Issues: Data quality with collection, validation, provenance

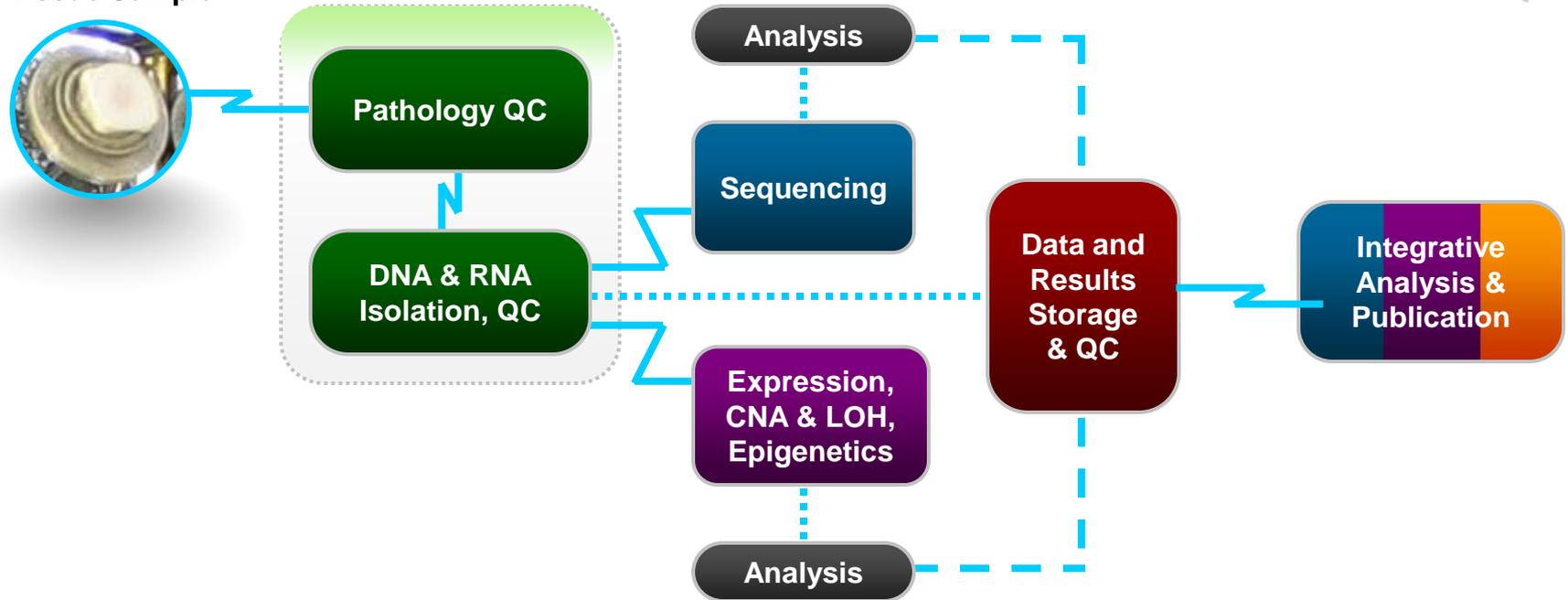
Data Status November 2011



TCGA: The Pipeline for Comprehensive Characterization



Tissue Sample



2012: The Year of TCGA Post-Pilot Publications



- Colorectal Cancer
- Acute Myeloid Leukemia
- Breast Cancer
- Endometrial Cancer
- Kidney Clear Cell
- Lung Adeno/Squamous
- Head and Neck Cancer
- Etc.

TCGA: Whole Genome Sequencing



Tumor Type	In Progress	Completed
GBM	-	22
Colorectal	15	5
Renal	-	10
Breast (triple negative)	1	20
AML	-	49
Ovarian	7	13
Endometrial (serous type)	28	2
LUSC	1	19
LUAD	14	6
<i>Total</i>	<i>66</i>	<i>146</i>

TCGA: Expanding the Enterprise



- Pilot project: FFPE-preserved tissues
- Pilot project: Mouse models of human cancers
- Projects to study rare tumor types (smaller numbers yet comprehensive focus of assays and analysis)
- Integration efforts: International Cancer Genomics Consortium
- Integration efforts: interface between TCGA (genomics of cancer samples) and CPTAC (proteomics of cancer samples)

mTCGA Committee Members

- Elaine Mardis (Chair)
- Tyler Jacks
- Monica Justice
- David Threadgill
- Allan Balmain
- Glenn Merlino
- Kenna Shaw (NCI)



mTCGA Pilot Projects



- Prostate cancer: Cory Abate-Shen
 - Models are based on a tamoxifen-inducible conditional allele, Nkx3.1CreErT2 (Wang et al., Nature 2009) crossed with a Pten floxed allele (Hong Wu) crossed with an activateable K-ras allele (Tyler Jacks).
 - Tumors are induced by administration of Tamoxifen in adult mice.
 - Phenotype: The mutant mice develop preinvasive lesions (called PIN) that progress to invasive cancer and ultimately metastatic disease. By 4 months of age, these mice display 100% penetrance of adenocarcinoma as well as 30% incidence of distant metastases. Tumors are epithelial in origin.
- Melanoma: Glenn Merlino
 - Melanoma model is driven by constitutive c-MET signaling and neonatal UV irradiation, and accelerated by loss of one Ink4a allele.
 - Mean latency is about 3-4 months to melanoma. Premalignant "spots" can be seen earlier. Metastasis can be seen in about 20% of the mice.

mTCGA Pilot Projects



- NSCLC: Christopher Kemp
 - A single injection of urethane is given to pre-weanling mice and tumors resembling non small cell adenomas and adenocarcinomas arise after a long latency.
 - >75% of all induced tumors contain activating mutations in Kras.
- Breast cancer: Muller, Green and Sharpless models
 - Green: Overexpression of PyMT in mammary epithelium results in highly aggressive tumor formation and metastases.
 - Sharpless: Classical MMTV-Neu GEMs (in 100% FVB/n) treated for 2-8 months with lapatinib and now resistant. Both resistant and sensitive tumors in-hand.
 - Muller: MMTV/Activated ErbB2 IRES Cre transgenic where ErbB2 expression is coupled to Cre mediated excision of any conditional allele.

Clinical Proteomic Tumor Analysis Consortium



- 5 teams funded to perform proteomic work in relationship to genomic discoveries from programs like TCGA
- First projects to look at genome-proteome correlations in breast (Matthew Ellis), Ovarian (Dan Chan) and Colorectal (Dan Liebler)
- Will receive portions of TCGA-characterized cases from BCRs to perform proteomic analysis (shotgun or targeted)
- Identifying validation samples from similar cohorts, blood samples for next phases

Next Steps



- Thank you for attending!
- We value your feedback to improve the meeting...
- Please look for announcements on the 2nd Annual TCGA Scientific Symposium!!