



# Simplifying and Systematizing Science at Unprecedented Scales & Complexity

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**Michael S. Noble**  
**Genome Data Analysis Center**  
**The Broad Institute of MIT & Harvard**

Cancer Genome Summit

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Boston, Massachusetts, USA



# Acknowledgements

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# OUTLINE

- I. Why Firehose
- II. TCGA Data Flow
- III. What Firehose produces
- IV. How To Get It

# I. WHY FIREHOSE?

Born of the desire to systematize analyses from The Cancer Genome Atlas pilot and scale their execution to the dozens of remaining diseases to be studied, now sits atop ~35 terabytes of TCGA data and reliably executes more than 2300 pipelines per month.





Because The Bad Old Days ...

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# Because The Bad Old Days ...

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Of solitary, manual experimentation on few dozen samples ...

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% create a folder
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```
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% run_your_computational_analysis
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Then do it again Nov 13, 17, ...

Then forget, search ... lose track, search ...

Then repeat ALL for 20 more tumors

GBM, LUNG, AML, ...



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GBM, LUNG, AML, ...

Then multiply by 5, 10 ... researchers at your site

# Don't Scale to TCGA

November 14, 2012  
Firehose Data Snapshot

Tumor	BCR	Clinical	CN	LowP	Methylation	mRNA	mRNAseq	miR	miRseq	RPPA	MAF
BLCA	153	108	99	0	138	0	96	0	124	54	28
BRCA	914	866	874	0	889	529	805	0	868	408	507
CESC	122	32	102	0	122	0	0	0	122	0	36
COAD	423	423	413	69	420	155	192	0	407	269	155
COADREAD	592	591	575	104	582	224	264	0	550	399	224
DLBC	28	0	17	0	17	0	0	0	16	0	0
GBM	598	565	563	0	411	542	161	491	0	214	276
HNSC	328	315	294	96	310	0	303	0	309	212	0
KICH	66	0	65	0	65	0	0	0	0	0	0
KIRC	502	502	493	0	500	72	469	0	480	454	403
KIRP	149	103	103	0	103	16	63	0	103	0	0
LAML	202	200	0	0	194	0	179	0	187	0	199
LGG	222	198	180	0	176	27	110	0	180	0	0
LIHC	99	62	97	0	98	0	17	0	96	0	0
LUAD	439	294	356	0	430	32	353	0	365	237	229
LUSC	376	327	343	0	359	154	223	0	332	195	178
OV	592	580	566	0	557	575	297	570	454	412	316
PAAD	57	0	48	0	40	0	0	0	34	0	0
PANCAN8	4086	3882	3907	210	3798	2150	2515	1061	3169	2282	2152
PRAD	180	127	171	0	172	0	140	0	170	0	83
READ	169	168	162	35	162	69	72	0	143	130	69
SARC	29	0	29	0	29	0	0	0	29	0	0
SKCM	273	138	253	101	253	0	247	0	240	164	0
STAD	238	162	144	0	145	0	43	0	134	0	116
THCA	435	218	330	94	353	0	254	0	349	224	323
UCEC	512	451	493	106	500	54	333	0	485	200	248
Totals	7106	5839	6195	501	6443	2225	4357	1061	5627	3173	3166



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**Diffs since Nov 2011  
(~11K samples)**



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**New data types  
(12.5K samples)**



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**Diffs since Nov 2011  
(~11K samples)**

**New data types  
(12.5K samples)**

**Last year: ~24K  
new samples**

# Acute Need for Automation, Systematic Rigor, and Transparency

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GDAC Firehose == Virtual Data Factory

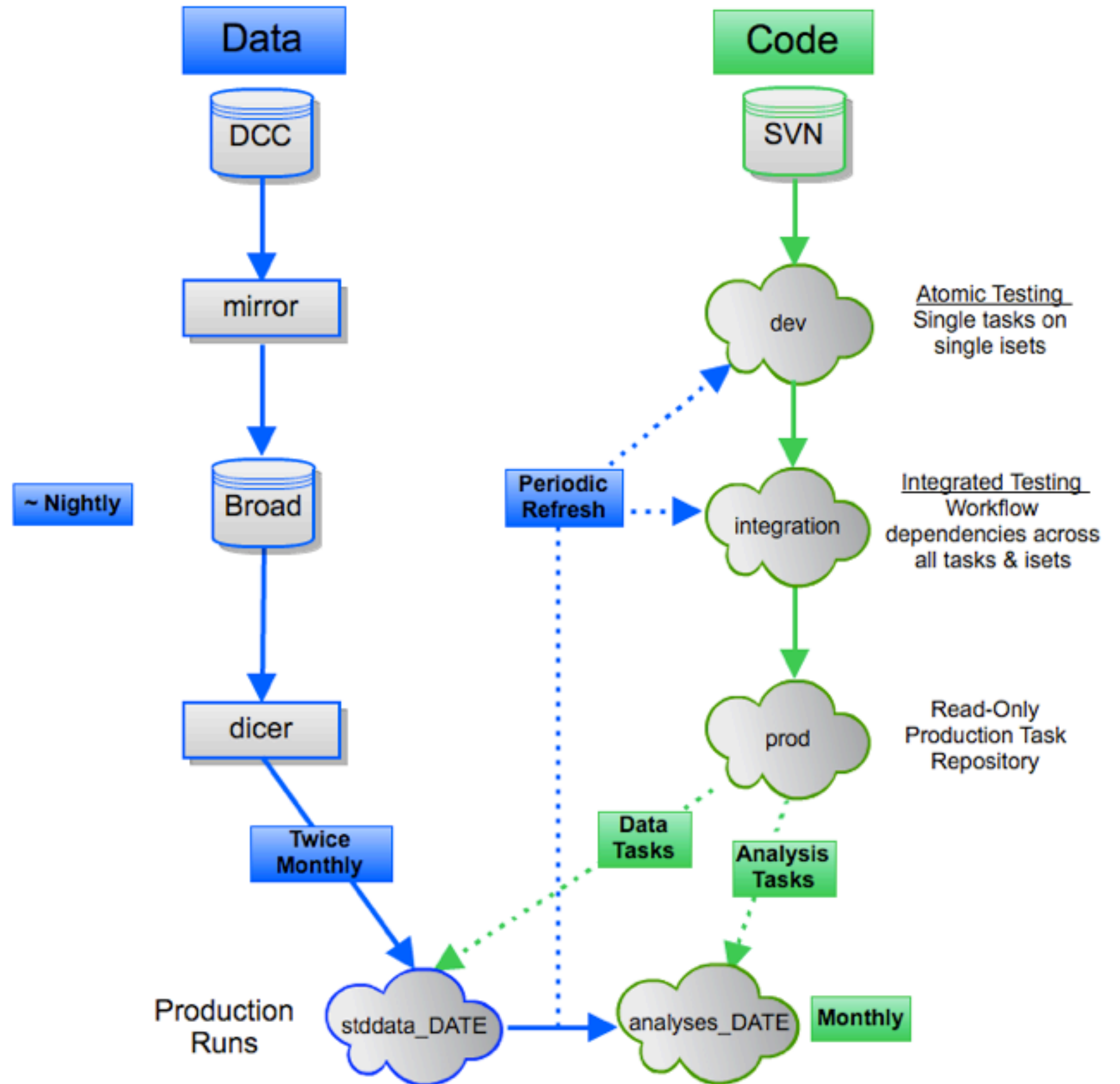


# Broad Institute TCGA GDAC Internal Process Flow

Version 2011\_04\_11

**Subject to Same Engineering Constraints of Timeliness, Transparency & Rigor as Physical Factories**

**Not academic one-off**



# II. TCGA NOVEMBER 2012 THE DATA FLOOD CONTINUES





# II. TCGA NOVEMBER 2012

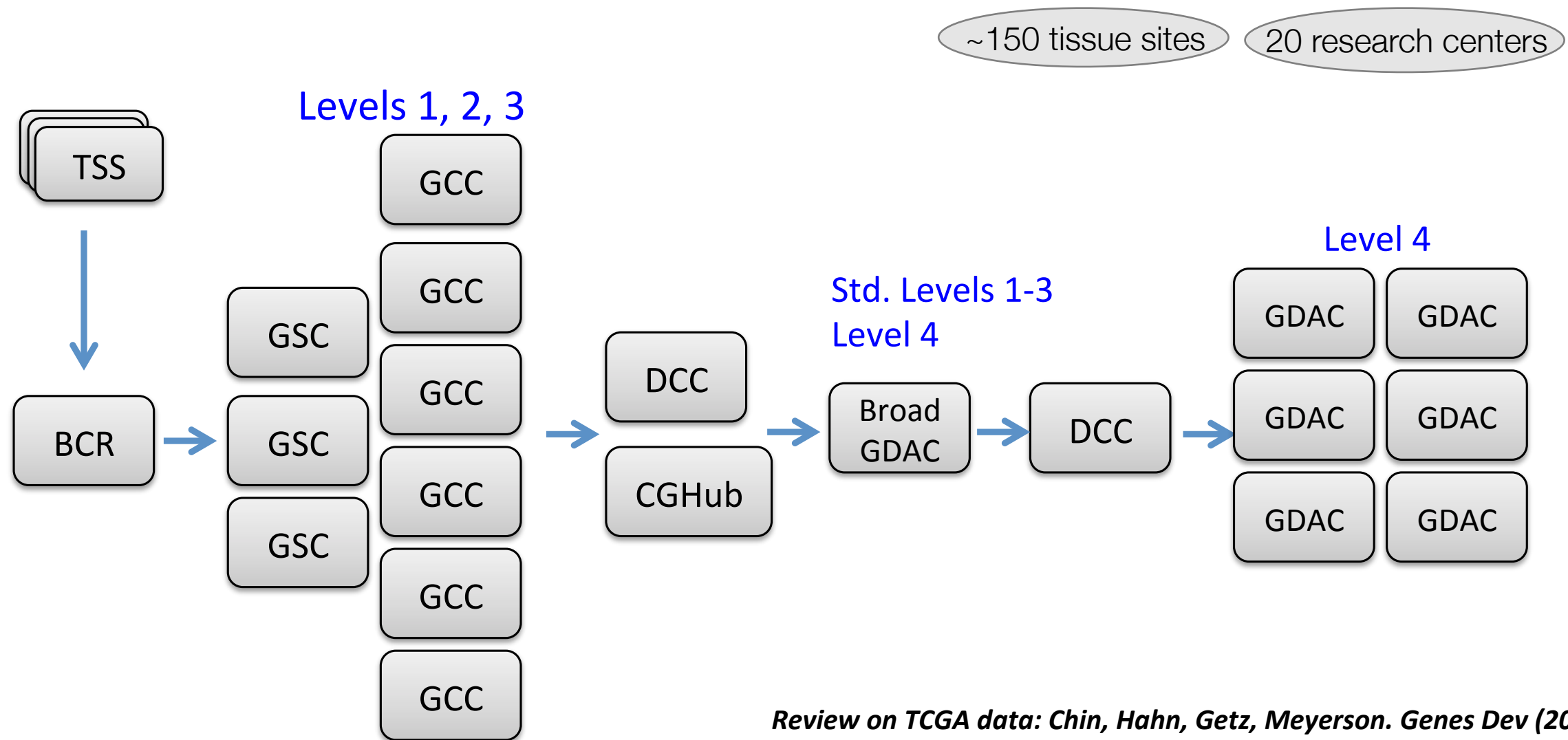
## THE DATA FLOOD CONTINUES



- 7K patient cases, heading to 11K total
- 26 tumor cohorts (plus clinical)
- 6 marker papers published, more underway
- Swirling amongst 20 centers nationwide (and ICGC)



# Understanding TCGA : data flow & levels



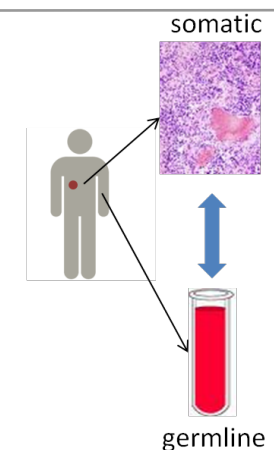
Review on TCGA data: Chin, Hahn, Getz, Meyerson. *Genes Dev* (2011)

## Purpose 1: Characterization:

**Level 1** – Raw data (e.g. raw reads and qualities, Affymetrix CEL files)

**Level 2** – Normalized data (e.g. aligned reads – BAM files, intensity matched files)

**Level 3** – Genomic events (e.g. somatic mutations, segments of copy number changes)

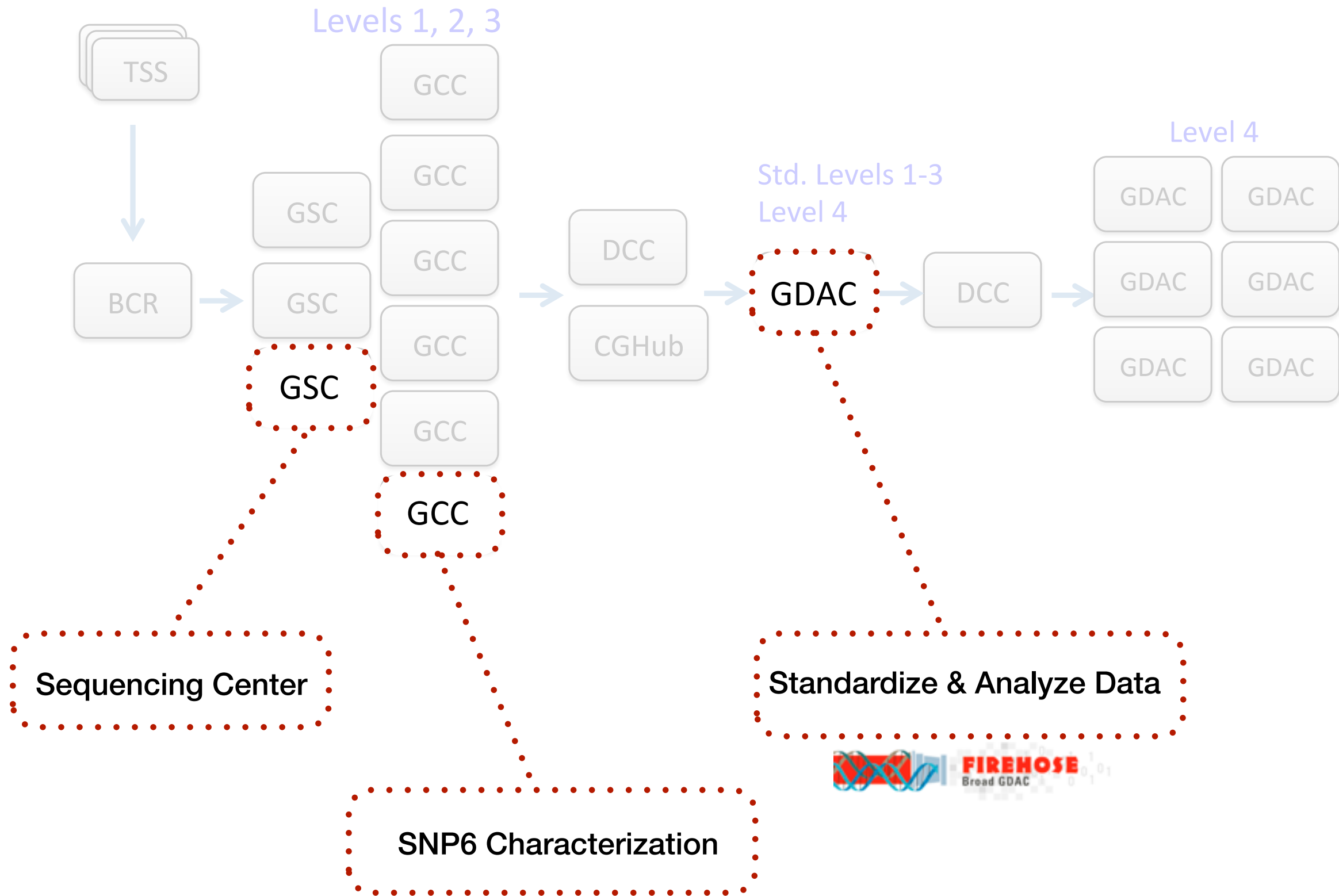


## Purpose 2: Interpretation:

**Level 4** – Analysis across a cohort (e.g. sub-types discovery, correlate data types, significantly mutated genes/regions/pathways, correlation to clinical parameters)



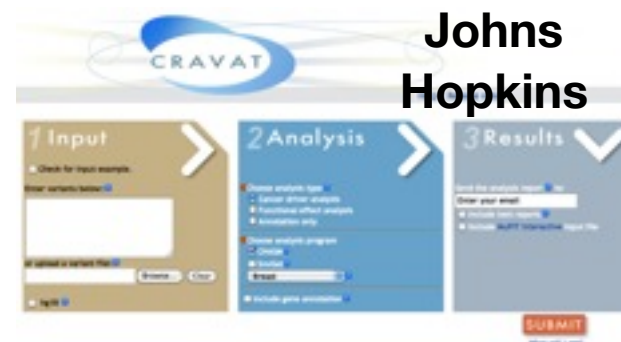
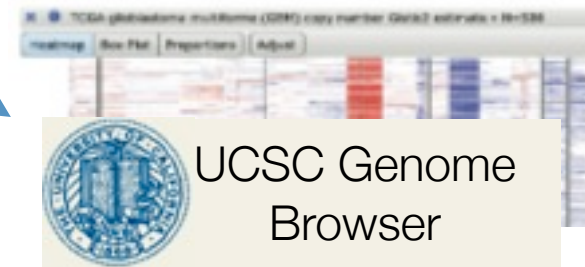
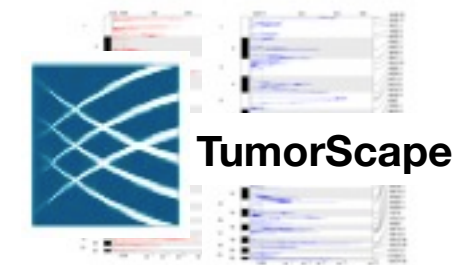
# Broad Contribution: 3 of 20 research centers



# Flowing Into Other Portals



stddata\_\_2012\_MM\_DD  
analyses\_\_2012\_MM\_DD



# BUT HOW IS DATA STREAM USED TO ANSWER COMMON BIOLOGICAL QUESTIONS?

- Such as:

Is my gene of interest altered in this tumor type? How?  
Is that alteration significantly above the background rate?  
How might those features map to clinical or molecular feature X?

- There is no one-size-fits-all, cookie-cutter method to answer such questions
- But some analyses are common to many questions and can be automated:
  - ▶ Mutation calling, classifying, summarizing and significance-testing
  - ▶ Copy number alteration detection and significance-testing
  - ▶ Expression- and methylation-based clustering
  - ▶ Associating genomic data with common clinical, treatment or survival groups



- These common results then become building blocks for higher-level analysis
- So downstream users do not have to repeat each time  
(e.g. automation a boon when 20 new samples added to 250)
- Nor perform ad-hoc reinvention of methods
- Nor download all low-level data from which they were generated
- Nor institute their own ad-hoc data freeze/versioning scheme
- ... to ensure accuracy & reproducibility of analytic/statistical results
- Nor institute ad-hoc QC program ... to minimize human error in large-data analyses

**Firehose aims to address such concerns, at scale,  
lowering the entry barrier for TCGA utilization**

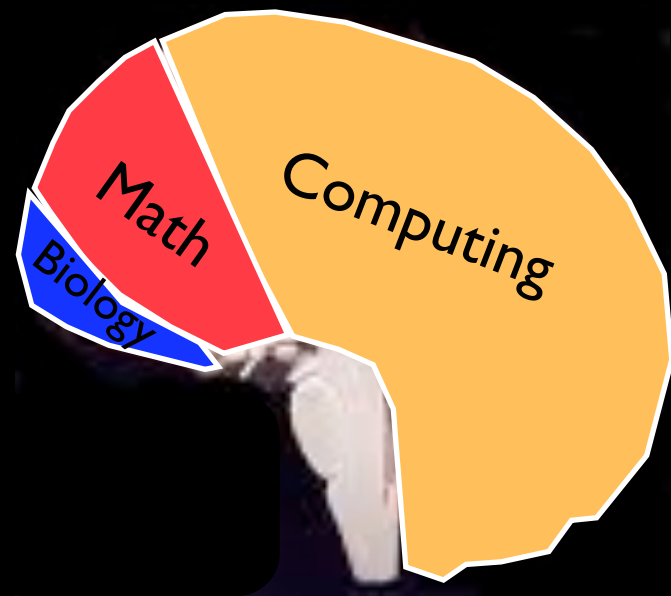
Must be Simple, Flexible, Easy ... because



This is Your  
Researcher  
Brain

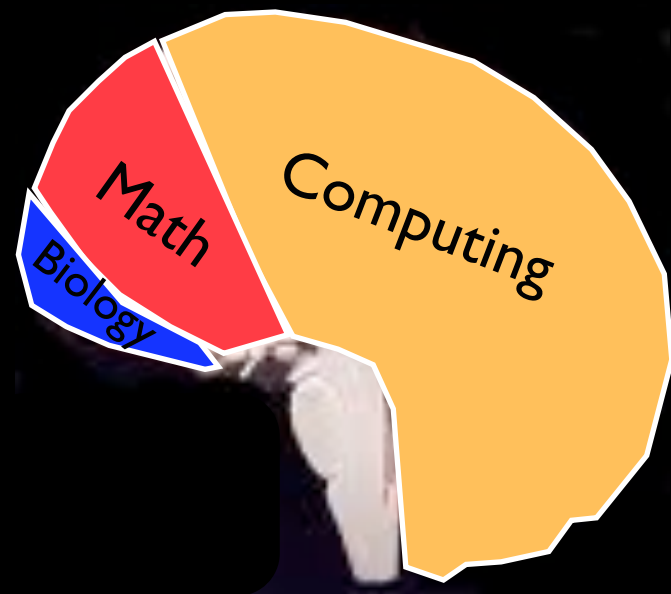


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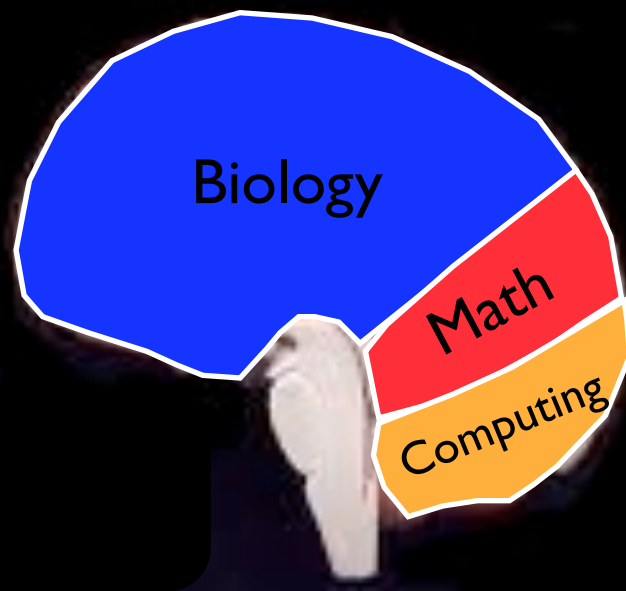


When Coding  
Or Data  
Exploration  
Is Hard

Must be Simple, Flexible, Easy ... because



When Coding  
Or Data  
Exploration  
Is Hard



When  
Easier

*Civilization advances by extending the number of important operations which we can perform without thought.*

A. North Whitehead



# III. So Firehose Data Factory Produces

---

- 1 Version-stamped, standardized datasets (2X / month)

*Precursor to automated analyses, durable (DCC) & citable  
Minimizing effect of **The Babel Problem***

- 2 Regular package of standard analyses results (1X / month)

*For vetted algorithms: GISTIC, MutSig, CNMF, ...*

- 3 Companioned with biologist-friendly reports (475 / month)

*Instantly up-to-speed on current TCGA results  
(zero time/budget/staff investment)*

# Both Archival & Active Research by TCGA AWGs

## 2012\_08\_25 awg\_pancan8 Analyses Run

Tables of Ingested Data: [HTML](#) [PNG](#) [TSV](#) Redactions: [Report](#)

AnalysisReport	# Pipelines	% Successful
<a href="#">BRCA</a>	35	<a href="#">100%</a>
<a href="#">COADREAD</a>	35	<a href="#">100%</a>
<a href="#">GBM</a>	34	<a href="#">100%</a>
<a href="#">KIRC</a>	35	<a href="#">100%</a>
<a href="#">LUSC</a>	35	<a href="#">100%</a>
<a href="#">OV</a>		
<a href="#">UCEC</a>		
<a href="#">PANCAN</a>		

### Analysis Overview for Thyroid Adenocarcinoma: 2012\_10\_24

Maintained by [TCGA GDAC Team](#) (Broad Institute/Dana-Farber Cancer Institute/Harvard Medical School)

Unique Tumor Sample Counts

Tumor	BCR	Clinical	CN	LowP	Methylation	mRNA	mRNAseq	miR	miRseq	RPPA	MAF
THCA	435	218	330	94	353	0	254	0	349	224	323

### Analysis Overview for Lung Adenocarcinoma: 2012\_11\_15

Maintained by [TCGA GDAC Team](#) (Broad Institute/Dana-Farber Cancer Institute/Harvard Medical School)

Unique Tumor Sample Counts

Tumor	BCR	Clinical	CN	LowP	Methylation	mRNA	mRNAseq	miR	miRseq	RPPA	MAF
LUAD	439	294	358	0	432	32	355	0	366	237	229

Download run results with [firehose\\_get version 0.3.8](#)

Download command: `firehose_get awg_luad 2012_11_15`

[Task Dashboard](#)

- Overview
- Introduction
- Summary

**Note:** These results are offered to the community as an additional reference point, enabling a wide range of cancer biologists, clinical investigators, and genome and computational scientists to easily incorporate TCGA into the backdrop of ongoing research. While every effort is made to ensure that Firehose input data and algorithms are of the highest possible quality, these analyses have not been reviewed by domain experts.

[firehose\\_get version 0.3.8](#)

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UCEC  
SKCM  
LUSC



# Unprecedented Scale: KiloPipeline per Month

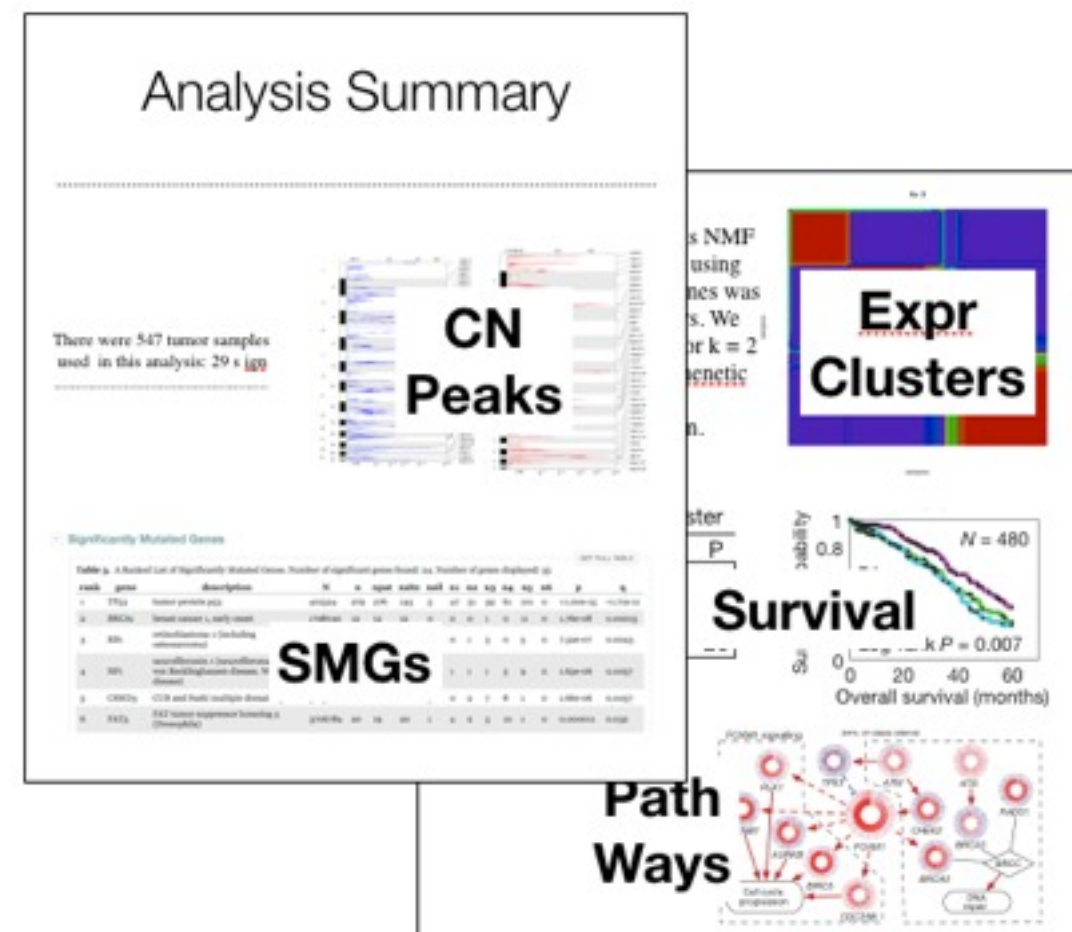
**stddata\_\_2012\_10\_04**  
**stddata\_\_2012\_10\_24**  
**analyses\_\_2012\_10\_24**

**547 datasets submitted to DCC**  
**940 datasets ...**  
**837 analyses ...**

**2324 pipelines across 26 disease cohorts**

*With up to 33  
biologist-friendly  
analysis reports  
per disease  
(475 reports in all)*

**Single Month: Oct 2012**



# Again: Not Mutually Exclusive With **“Easy”**

---

% gdac_diff	2012_09_13	2012_10_04	\$PANCAN8
mRNAseq	+161	(2304 total)	
CN	+125	(3907 total)	
Methylation	+30	(3667 total)	
Clinical	+30	(3864 total)	
BCR	+16	(4086 total)	

2 seconds to understand sample diffs in 35+ terabytes

***Version stamp: rigor & clarity → ease***



# Easy Corroboration: first-pass, low hanging fruit

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- Enable readers (PIs, bench bios, clinical trialists, DotComs)
- To quickly take pulse of TCGA for given disease type(s)
- With just a few glances at common representational figures
- Not deep head-scratching or big time investment

“Oh, that’s interesting, maybe my code has found something here ... I wonder if this is seen in the Firehose version **2012\_07\_25** results, too?”

Durability of DCC archive fosters citable referencing:

“Our analyses were performed against TCGA dataset version **2012\_07\_25** and validated against ...”

# BUT MIND THE FINE PRINT

These results are offered to the community as an additional reference point, enabling a wide range of cancer biologists, clinical investigators, and genome & computational scientists to easily incorporate TCGA into the backdrop of ongoing research.

STARTING POINT : NOT FINAL WORD

AUTOMATIC MACHINES ARE DUMB & IMPERFECT

EXPERT JUDGEMENT STILL REQUIRED



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`firehose2nature` tool is organic, not in-silico

# Future Potential: Automated Clinical Gold Mine?

---

Wealth of clinical data collected by TCGA

To date underrepresented in TCGA-based publications

Understandable byproduct of complex mix of

scientific, technological & operational factors

But clear steps can be taken to minimize extent that

Sheer volume & complexity ... **alone** ...

Impede fuller exploitation of clinical in TCGA-based work

Firehose automatically mines entire suite of clinical params to identify statistically significant relationships with every TCGA datatype or aggregate (e.g. clusters)

The results, which e.g. include survival curves (when possible) for every TCGA disease, are posted openly on the Broad GDAC site in the form of biologist-friendly HTML reports

Since automation is free, these don't have to be 100% to establish potentially interesting signposts



# Precedent in 2011 Ovarian Manuscript

---

Given richness of TCGA data stream,  
Discoveries lurk in our GDAC pipeline outputs

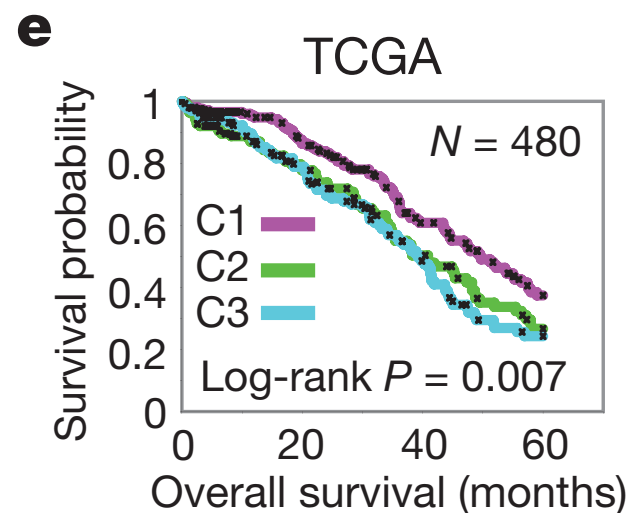
# Precedent in 2011 Ovarian Manuscript

---

**d**

		Gene cluster			
		D	I	M	P
miRNA cluster	C1	55	48	15	89
	C2	40	21	51	29
	C3	39	37	43	20

CNMF clustering of OV miR expression yielded 3 subtypes

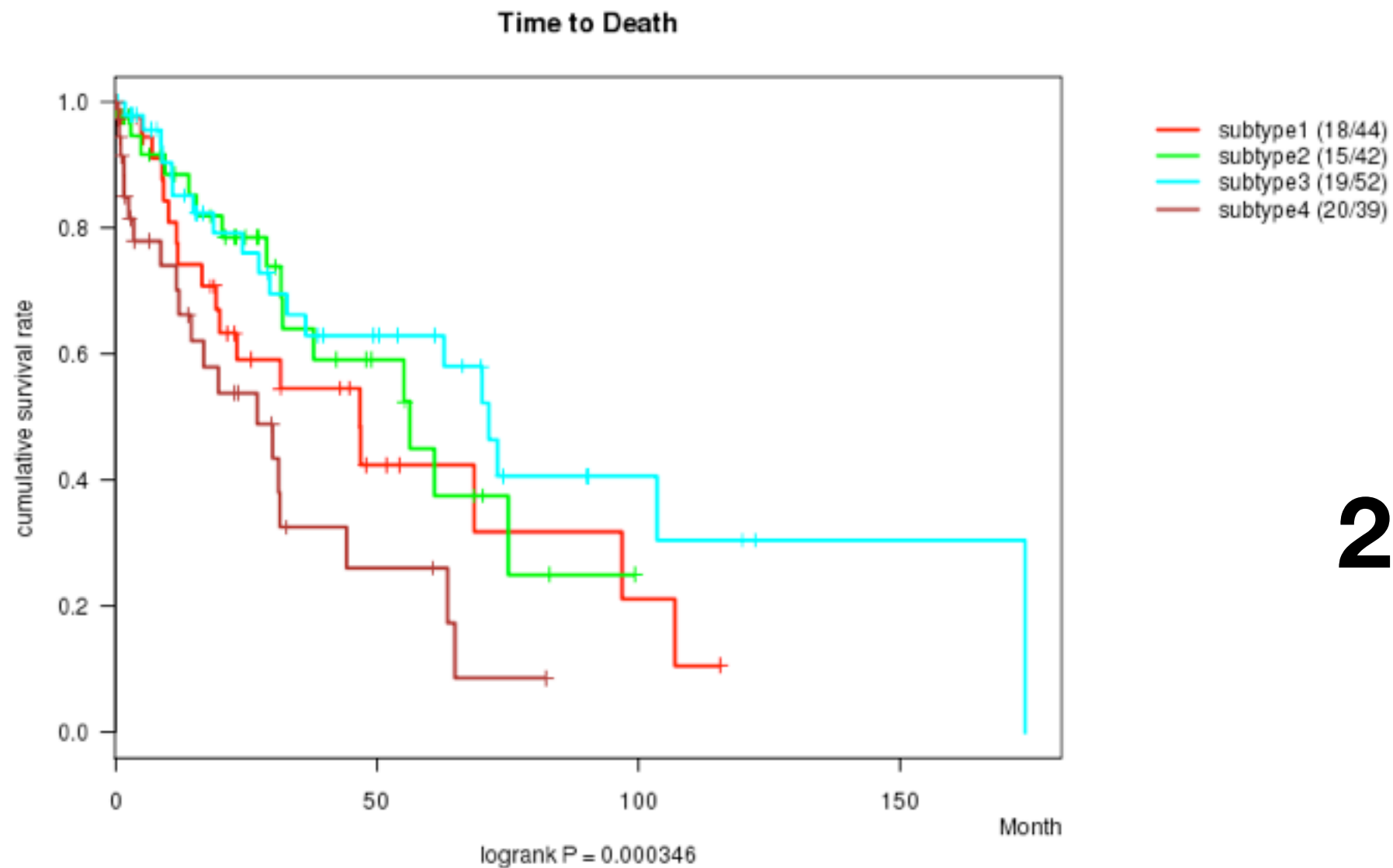


One of which correlated to significantly longer survivability

***Integrated genomic analyses of ovarian carcinoma  
TCGA Network, Nature, June 2011***

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# LUSC



**2012\_09\_13**  
**Analyses**

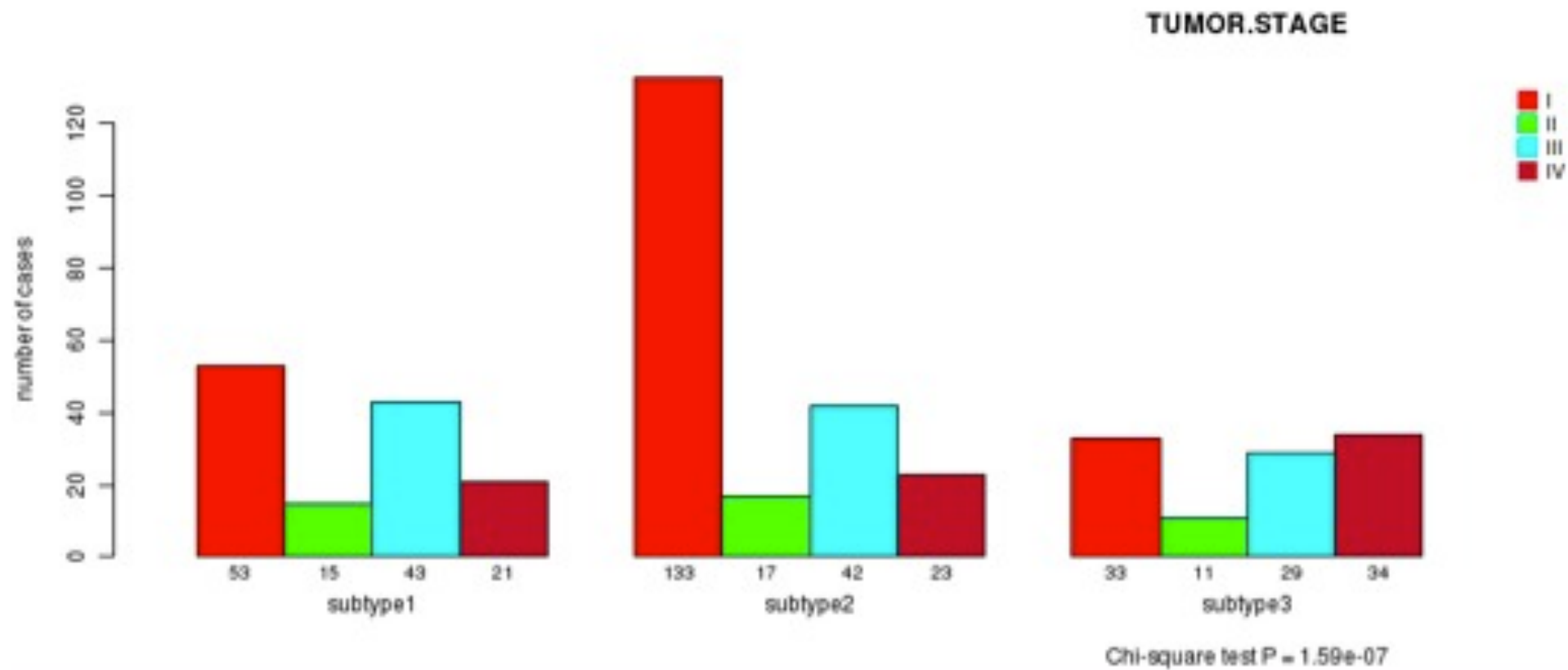
	nPatients	nDeath	Duration Range (Median), Month
<b>ALL</b>	<b>177</b>	<b>72</b>	<b>0.0 - 173.8 (16.6)</b>
subtype1	44	18	0.2 - 115.6 (14.3)
subtype2	42	15	0.2 - 99.2 (23.0)
subtype3	52	19	0.0 - 173.8 (17.8)
subtype4	39	20	0.1 - 82.2 (8.8)

*'RPPA cHierClus subtypes' versus 'Time to Death'*

P value = 0.000346 (logrank test)



# KIRC



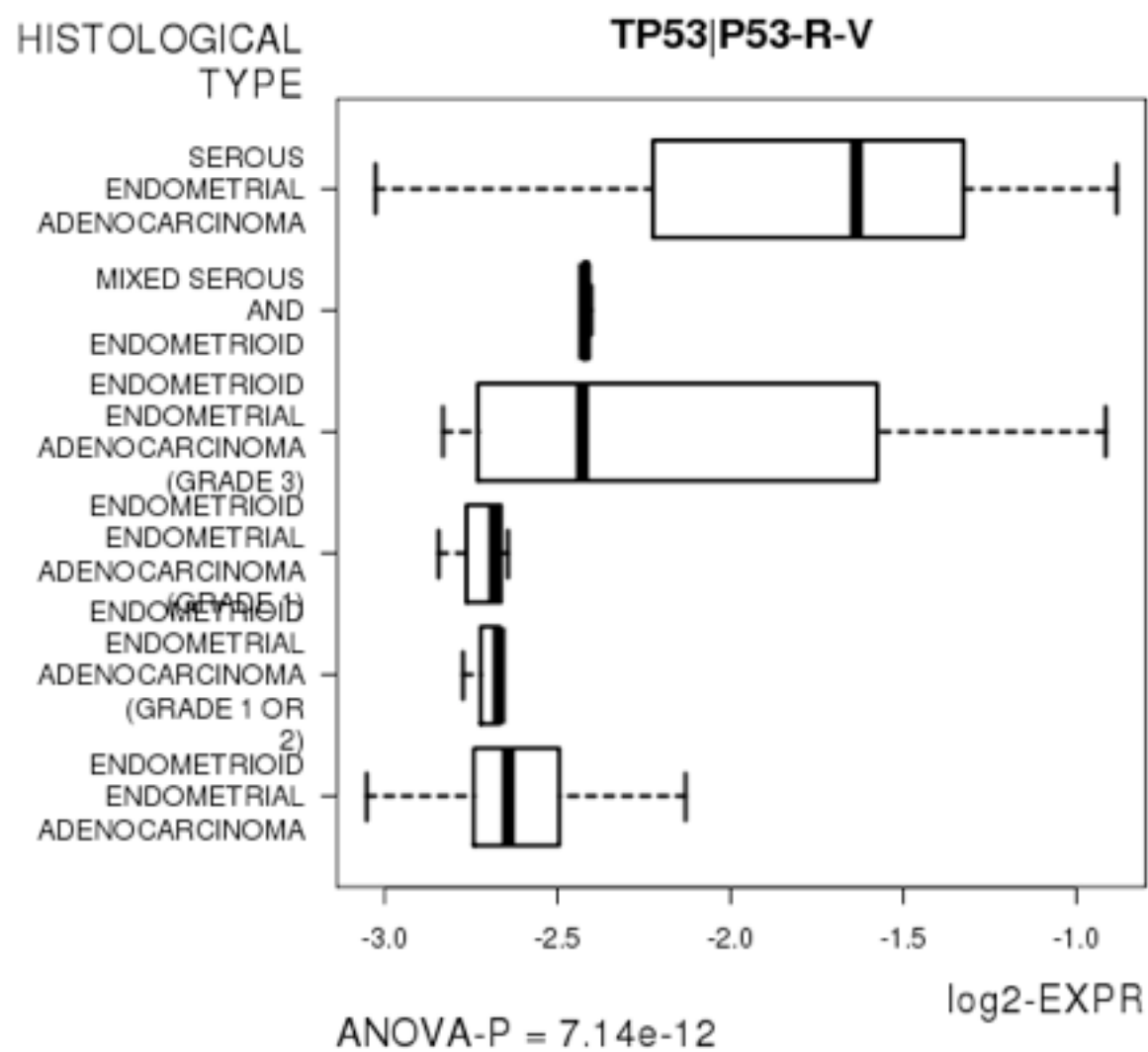
nPatients	I	II	III	IV
<b>ALL</b>	<b>219</b>	<b>43</b>	<b>114</b>	<b>78</b>
subtype1	53	15	43	21
subtype2	133	17	42	23
subtype3	33	11	29	34

'RPPA cHierClus subtypes' versus 'TUMOR.STAGE'

P value = 1.59e-07 (Chi-square test)

# UCEC

Correlation between RPPA expression and '*HISTOLOGICAL.TYPE*'



	ANOVA_P	Q
<a href="#">TP53 P53-R-V</a>	7.144e-12	1.19e-09
<a href="#">CHEK2 CHK2_PT68-R-C</a>	7.824e-09	1.29e-06
<a href="#">AKT1 AKT2 AKT3 AKT_PS473-R-V</a>	6.908e-08	1.13e-05
<a href="#">PGR PR-R-V</a>	1.307e-07	2.13e-05
<a href="#">CDC2 CDK1-R-V</a>	2.576e-07	4.17e-05
<a href="#">CDH1 E-CADHERIN-R-V</a>	2.644e-07	4.26e-05
<a href="#">ESR1 ER-ALPHA-R-V</a>	9.567e-07	0.000153
<a href="#">ESR1 ER-ALPHA_PS118-R-V</a>	3.992e-06	0.000635
<a href="#">EEF2 EEF2-R-V</a>	7.75e-06	0.00122
<a href="#">EIF4EBP1 4E-BP1_PS65-R-V</a>	1.874e-05	0.00294

# IV. How To Access

2012\_10\_24 stddata Run

DiseaseType	# Datasets	% Processed	Download
BLCA	38	100%	Open Protected
BRCA	48	100%	Open Protected
CESC	20	100%	Open Protected
COADREAD	38	100%	Open Protected
COAD	38	100%	Open Protected
DLBC	13	100%	Open Protected
GBM	51	100%	Open Protected
HNSC	40	100%	Open Protected
KICH			Open Protected
KIRC			Open Protected
KIRP			Open Protected
LAML			Open Protected
LGG			Open Protected
LIHC			Open Protected
LUAD			Open Protected
LUSC			Open Protected
OV	57	100%	Open Protected
PAAD	14	100%	Open Protected
PRAD	30	100%	Open Protected
READ	38	100%	Open Protected
SARC	13	100%	Open Protected
SKCM	24	100%	Open Protected
STAD	27	100%	Open Protected
THCA	40	100%	Open Protected
UCEC	48	100%	Open Protected
PANCANB	87	95%	Open Protected

Data  
Dashboard

2012\_10\_24 analyses Run

AnalysisReport	# Pipelines	% Successful	Download
BLCA	36	100%	Open Protected
BRCA	44	100%	Open Protected
CESC	26	100%	Open Protected
COADREAD	44	100%	Open Protected
COAD	44	100%	Open Protected
GBM	46	100%	Open Protected
HNSC	18	100%	Open Protected
KIRC	44	100%	Open Protected
KIRP			Open Protected
LAML			Open Protected
LGG			Open Protected
LIHC			Open Protected
LUAD			Open Protected
LUSC			Open Protected
OV			Open Protected
PAAD			Open Protected
PRAD	33	100%	Open Protected
READ	44	100%	Open Protected
SARC	7	100%	Open Protected
SKCM	25	100%	Open Protected
STAD	31	100%	Open Protected
THCA	37	100%	Open Protected
UCEC	44	100%	Open Protected
DLBC	7	88%	Open Protected
KICH	6	75%	Open Protected
PANCANB	9	56%	Open Protected

Analysis  
Dashboard

<http://gdac.broadinstitute.org>

Open Public Resource

Interactive Desktop Use



# Nexus Resource for Evolving Community

---

- Thousands of views, 140K+ hits / month
- Hundreds of GB downloads / month
- Across dozens of centers & portals
- Research / Academic / Commercial
- National & International
- Beyond genomics : e.g. CPTAC / proteomics

# With Open (-Source) / Transparent Look & Feel

---

**Q: Why does your [table of ingested data](#) show that *disease type XYZ* has *N* mutation samples?**

**A:** Our precedence rules for ingesting mutation samples are:

1. Prefer manually-curated MAF from the respective analysis working group (AWG), on the premise that
2. When no AWG MAF is available, fall back to using what is available in the DCC by automatic subn
3. Otherwise Firehose will contain zero mutation samples for that disease type.

We're in the process of defining a fourth rule, however, to account for the evolving nature of TCGA mutati  
accrue at the DCC (again, automatically submitted by the respective GSCs), and it is natural for analysts

For more information, please consult [our provenance table for mutation data](#), the [TCGA MAF workflow](#) and  
will likely support VCFs once they become sufficiently prevalent in the TCGA dataflow.

**Q: Why does your [table of ingested data](#) show that *disease type XYZ* has *N* methylation samples?**

**A:** We ingest and support both of the major methylation platforms (meth450 and meth27), therefore the  
statistical algorithms used by TCGA AWGs to merge both of these methylation platforms into a single bol  
higher resolution data.

**Q: What TCGA sample types are Firehose pipelines executed upon?**

**A:** Since inception Firehose analyses have been executed upon tumor samples and then correlated with  
exception is [melanoma \(SKCM\)](#), which we analyze using metastatic tumor samples (code 06) as it is usu  
*we will include a larger range of sample types, including normals.*

**Q: What do you do when multiple aliquot barcodes exist for a given sample/portion/analyte comb**

**A:** To date GDAC analyses have proceeded upon one single tumor sample per patient, so when multiple  
metrics, we use the following rules to make such selections:

1. Prefer B aliquots over T when DNA aliquots of both type exist

## FAQ



## Re: [GDAC-users] firehose - download normal expression values

Subject: **Re: [GDAC-users] firehose - download normal expression values** ([find more](#))  
From: David Tamborero <hidden> ([find more](#))  
Date: Aug 26, 2012 14:22

Thank you very much, your work and help is priceless.

2012/8/24 Michael S. Noble <hidden>

>  
> Dear David,  
>  
> Apologies for the delay in responding. Yes, you are right: our outputs do  
> not  
> contain normals. This is partly a legacy held over from the TCGA pilot  
> studies, which is where many of the analyses in our GDAC originally stem  
> from. Our FAQ online at [gdac.broadinstitute.org](http://gdac.broadinstitute.org) discusses this in the  
> section  
>  
> Q: What TCGA sample types are Firehose pipelines executed upon?  
>  
> and points out that we aim to support normals in the Fall of 2012.  
>  
> Regards,  
> Mike Noble  
>

# Searchable Mail Archive





## Re: [GDAC-users] firehose - download normal expression values

Subject: Re: [GDAC-users] firehose - download normal expression values ([find more](#))  
 From: David Tamborero <hidden> ([find more](#))  
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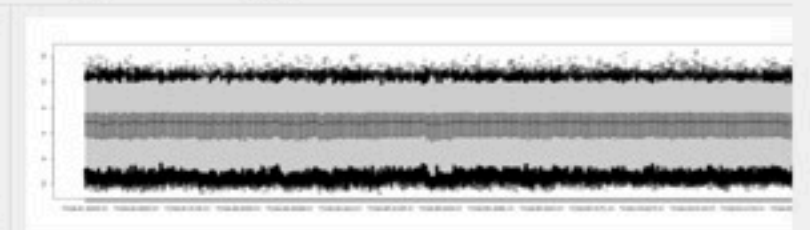
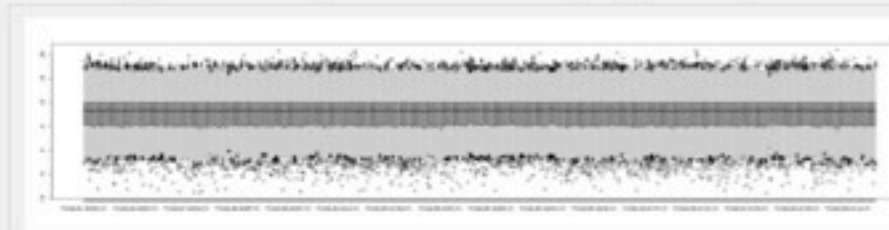
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 >  
 > and points out that we aim to support normals in the  
 >  
 > Regards,  
 > Mike Noble  
 >

# Searchable Mail Archive

June 2012 (2012\_06\_23)

1. Increased number of archives generated from 777 to 993
2. Increased number of reports from 227 to 252
3. 2,244 new samples reflected since May analyses run, due to more data and better counting:
  - 76 LowP (new sample type - Low Pass DNaseq)
  - 230 BCR
  - 307 Clinical
  - 618 mRNAseq
  - 937 miRseq
  - 76 MAF
4. GISTIC2 report now includes a description of both the input and output files in the *Methods & Data* section
5. Methylation data:
  - Rewired pipelines to include meth450 platform, and also give it preference over meth27 when both are present. (Methods to combine 450 & 27 analytically are not in Firehose: would be nice for AWGs to provide if possible)
  - This greatly increases count of methylation samples flowing through analyses (e.g. UCEC 117-->363)
  - Most clusterings show similar results, but some are discordant with previous runs: we could use AWG help to evaluate, and will post comparative analysis online towards that end
6. New clustering pipelines heuristic: a sample will be dropped from analyses when 80% or more genes are absent.
7. mRNAseq: we now utilize maseqv2 archives, but fall back to v1 maseq when v2 is not available for a given tumor type
  - RSEM estimation used for downstream clustering & correlation analysis, when available, otherwise RPKM estimation will be used
  - RSEM is used to estimate gene and transcript abundances (<http://deweylab.biostat.wisc.edu/rsem/rsem-calculate-expression.html>); values are normalized to a fixed upper quartile value of 1000 for gene and 300 for transcript level estimates, and the normalized values are placed in a separate file (From the DCC document).
  - The following showed the boxplot of BRCA mRNAseq samples with log2 transformed RESM (left) and RPKM (right).



# Detailed Release Notes

# stddata dashboard

The Broad GDAC standardized data packages represent a frozen snapshot of all [TCGA](#) analysis data at a given time:

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- Which provides a **consistent point of reference** for analysis and [citation by marker papers and users](#) of TCGA data
- Towards a **formal definition** of what constitutes a given tumor dataset
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## 2012\_08\_04 stddata Run

Tables of Ingested Data: [HTML](#) [PNG](#) [TSV](#) Redactions: [Report](#)

ReleaseNotes	# Datasets	% Processed	Download	
<a href="#">BLCA</a>	20	<a href="#">100%</a>	<a href="#">Open</a>	<a href="#">Protected</a>
<a href="#">BRCA</a>	27	<a href="#">100%</a>	<a href="#">Open</a>	<a href="#">Protected</a>
<a href="#">CESC</a>	11	<a href="#">100%</a>	<a href="#">Open</a>	<a href="#">Protected</a>
<a href="#">COADREAD</a>	21	<a href="#">100%</a>	<a href="#">Open</a>	<a href="#">Protected</a>
<a href="#">DLBC</a>	5	<a href="#">100%</a>	<a href="#">Open</a>	<a href="#">Protected</a>
<a href="#">GBM</a>	27	<a href="#">100%</a>	<a href="#">Open</a>	<a href="#">Protected</a>
<a href="#">HNSC</a>	20	<a href="#">100%</a>	<a href="#">Open</a>	<a href="#">Protected</a>
<a href="#">KIRC</a>	27	<a href="#">100%</a>	<a href="#">Open</a>	<a href="#">Protected</a>
<a href="#">KIRP</a>	23	<a href="#">100%</a>	<a href="#">Open</a>	<a href="#">Protected</a>
<a href="#">LAML</a>	11	<a href="#">100%</a>	<a href="#">Open</a>	<a href="#">Protected</a>
<a href="#">LGG</a>	17	<a href="#">100%</a>	<a href="#">Open</a>	<a href="#">Protected</a>
<a href="#">LIHC</a>	17	<a href="#">100%</a>	<a href="#">Open</a>	<a href="#">Protected</a>
<a href="#">LUAD</a>	26	<a href="#">100%</a>	<a href="#">Open</a>	<a href="#">Protected</a>
<a href="#">LUSC</a>	34	<a href="#">100%</a>	<a href="#">Open</a>	<a href="#">Protected</a>
<a href="#">OV</a>	32	<a href="#">100%</a>	<a href="#">Open</a>	<a href="#">Protected</a>
<a href="#">PAAD</a>	6	<a href="#">100%</a>	<a href="#">Open</a>	<a href="#">Protected</a>
<a href="#">PRAD</a>	16	<a href="#">100%</a>	<a href="#">Open</a>	<a href="#">Protected</a>
<a href="#">SKCM</a>	14	<a href="#">100%</a>	<a href="#">Open</a>	<a href="#">Protected</a>
<a href="#">STAD</a>	18	<a href="#">100%</a>	<a href="#">Open</a>	<a href="#">Protected</a>
<a href="#">THCA</a>	18	<a href="#">100%</a>	<a href="#">Open</a>	<a href="#">Protected</a>
<a href="#">UCEC</a>	22	<a href="#">100%</a>	<a href="#">Open</a>	<a href="#">Protected</a>
<a href="#">PANCANCER</a>	48	<a href="#">87%</a>	<a href="#">Open</a>	<a href="#">Protected</a>



# stddata dashboard

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Data/Provenance Rigor

Towards solving  
**BABEL Problem**

Launch Point For  
Analysis-Ready  
TCGA Data



ICGC, too!



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Data/Provenance Rigor

Towards solving  
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Launch Point For  
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ICGC, too!

# stddata\_\_2012\_11\_14 Samples Summary Report

## Overview

### Introduction

For TCGA data, redaction is the removal of cases from the data prior to publication or release. Redacted cases are generally rare, but cases must be redacted when the TSS/BCR subject link is incorrect ("unknown patient identity"), or in the case of genotype mismatch, completely wrong cancer, or completely wrong organ/tissue. Redaction occurs regardless of a case's analyte characterization or DCC data deposition status.

Rescission is the removal of samples from the list of redactions. This happens if the reason for redaction is eventually cleared up. For clarity, rescinded redactions do not appear in this report.

### Summary

There were 60 redactions.

## Results

### Redactions

Table 1.

Barcode	UUID	Date	Type	Notes
TCGA-BR-4190	282e979d-4ad9-4d42-8ffa-7487a94fa1f3	11/08/2012	STAD	Site found that there was duplicate tissue in their biobank with another ID and different clinical data than that sent to TCGA. Case is being redacted but may be salvaged if the site can reconcile the correct clinical data to the tissue.
TCGA-BR-4194	2c650fe1-48b0-4f88-bc11-04096be48571	11/08/2012	STAD	Site found that there was duplicate tissue in their biobank with another ID and different clinical data than that sent to TCGA. Case is being redacted but may be salvaged if the site can reconcile the correct clinical data to the tissue.
TCGA-BR-4195	7917234c-63be-4320-b7af-535381f99d99	11/08/2012	STAD	Site found that there was duplicate tissue in their biobank with another ID and different clinical data than that sent to TCGA. Case is being redacted but may be salvaged if the site

**Rigor, Transparency, Ease**  
**Comprehensive**  
**report on ingested samples**  
**From online dashboard**



# stddata\_\_2012\_11\_14 Samples Summary Report

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Rigor, Transparency, Ease

**Comprehensive  
report on ingested samples**

**From online dashboard**

Nov 8  
STAD  
redactions



# Clear disposition of every ingested sample, every run

- + Redactions
- + Blacklisted Samples
- Filtered Samples

GET FULL TABLE

**Table 3.** Click on any filtered samples count to display a table detailing the filtered samples for the associated tumor type.

Tumor Type	Filtered Samples Count
BLCA	<a href="#">40</a>
BRCA	<a href="#">693</a>
CESC	<a href="#">9</a>
COAD	<a href="#">1080</a>
DLBC	<a href="#">18</a>
GBM	<a href="#">930</a>
HNSC	<a href="#">602</a>
KIRC	<a href="#">923</a>
KIRP	<a href="#">209</a>
LIHC	<a href="#">222</a>
LUAD	<a href="#">930</a>
LUSC	<a href="#">726</a>
OV	<a href="#">658</a>
PRAD	<a href="#">548</a>
READ	<a href="#">157</a>
SARC	<a href="#">30</a>
SKCM	<a href="#">35</a>
STAD	<a href="#">274</a>
THCA	<a href="#">242</a>
UCEC	<a href="#">122</a>

- + Redactions
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Clear disposition of every ingested sample, every run

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Downloadable as TSV

Clear disposition of every ingested sample, every run

- + Redactions
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KIRP	<a href="#">209</a>
LIHC	<a href="#">222</a>
LUAD	<a href="#">930</a>
LUSC	<a href="#">726</a>
OV	<a href="#">658</a>
PRAD	<a href="#">548</a>
READ	<a href="#">157</a>
SARC	<a href="#">30</a>
SKCM	<a href="#">35</a>
STAD	<a href="#">274</a>
THCA	<a href="#">242</a>
UCEC	<a href="#">122</a>

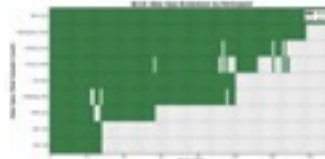
Downloadable as TSV

Or view heatmap figure

Sample Heatmaps

BLCA

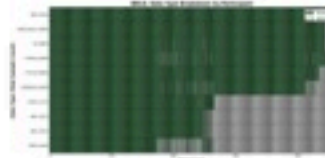
Figure 1. This figure depicts the distribution of available data on a per participant basis.



GET HIGH-RES IMAGE

BRCA

Figure 2. This figure depicts the distribution of available data on a per participant basis.



GET HIGH-RES IMAGE

CESC



# analysis dashboard

## 2012\_07\_25 analyses Run

Tables of Ingested Data: [HTML](#) [PNG](#) [TSV](#)

AnalysisReport	# Pipelines	% Successful	Download
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<a href="#">PAAD</a>	4	<a href="#">80%</a>	<a href="#">Open</a> <a href="#">Protected</a>
<a href="#">PANCANCER</a>	8	<a href="#">41%</a>	<a href="#">Open</a> <a href="#">Protected</a>

# analysis dashboard

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Tumor	BCR	Clinical	CN	LowP	Methylation	mRNA	mRNAseq	miR	miRseq	RPPA	MAF
BLCA	126	67	58	0	78	0	56	0	88	0	28
BRCA	899	862	833	0	858	529	777	0	809	408	507
CESC	122	31	68	0	0	0	0	0	42	0	36
COADREAD	592	591	575	76	584	224	83	0	255	399	224
DLBC	27	0	0	0	0	0	0	0	0	0	0
GBM	596									214	276
HNSC	312									0	0
KICH	65									0	0
KIRC	502									454	403
KIRP	135									0	0
LAML	202									0	199
LOG	181									0	0
LIHC	99									0	0
LNNH	2									0	0
LUAD	439									0	229
LUSC	360									0	178
OV	592	580	564	0	551	568	297	564	454	412	316
PAAD	48	0	14	0	30	0	0	0	0	0	0
PRAD	174	127	100	0	153	0	53	0	81	0	83
SARC	29	0	0	0	0	0	0	0	0	0	0
SKCM	253	129	219	0	240	0	212	0	240	0	0
STAD	226	159	132	0	133	0	57	0	127	0	133
THCA	353	188	228	0	230	0	158	0	138	0	0
UCEC	512	451	430	0	451	54	266	0	367	200	248
PANCANCER	6846	5633	5386	76	5465	2218	3460	1055	3976	2087	2860

Sample Counts  
(tabular/programmatic too)



# analysis dashboard

## 2012\_07\_25 analyses Run

Tables of Ingested Data: [HTML](#) [PNG](#) [TSV](#)

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Sample Counts  
(tabular/programmatic too)

Pipeline	NotRunnable	Runnable	InProcess	Successful	Unsuccessful
1 Aggregate_Clusters	0	0	0	1	0
2 CopyNumber_GeneBySample	0	0	0	1	0
3 CopyNumber_Gistic2	0	0	0	1	0
4 Correlate_Clinical_vs_CopyNumber_Arm	0	0	0	1	0
5 Correlate_Clinical_vs_CopyNumber_Focal	0	0	0	1	0
6 Correlate_Clinical_vs_miR	0	0	0	1	0
7 Correlate_Clinical_vs_Molecular_Signatures	0	0	0	1	0
8 Correlate_Clinical_vs_mRNA	0	0	0	1	0
9 Correlate_Clinical_vs_Mutation	0	0	0	1	0
10 Correlate_CopyNumber_vs_miR	0	0	0	1	0
11 Correlate_CopyNumber_vs_mRNA	0	0	0	1	0
12 Correlate_CopyNumber_vs_mRNAseq	0	0	0	1	0
13 Correlate_Methylation_vs_mRNA	0	0	0	1	0
14 Methylation_Clustering_CNMF	0	0	0	1	0
15 Methylation_Preprocess	0	0	0	1	0
16 miRseq_Clustering_CNMF	0	0	0	1	0
17 miRseq_Clustering_Consensus	0	0	0	1	0
18 miRseq_Preprocess	0	0	0	1	0
19 miR_Clustering_CNMF	0	0	0	1	0
20 miR_Clustering_Consensus	0	0	0	1	0
21 miR_FindDirectTargets	0	0	0	1	0
22 miR_Preprocess	0	0	0	1	0
23 mRNAseq_Clustering_CNMF	0	0	0	1	0
24 mRNAseq_Clustering_Consensus	0	0	0	1	0
25 mRNAseq_Preprocess	0	0	0	1	0
26 mRNA_Clustering_CNMF	0	0	0	1	0
27 mRNA_Clustering_Consensus	0	0	0	1	0
28 mRNA_Preprocess_Median	0	0	0	1	0
29 Mutation_Assessor	0	0	0	1	0
30 Mutation_Significance	0	0	0	1	0
31 Pathway_FindEnrichedGenes	0	0	0	1	0
32 Pathway_Paradigm_Expression	0	0	0	1	0
33 Pathway_Paradigm_Expression_CopyNumber	0	0	0	1	0
34 RPPA_Clustering_CNMF	0	0	0	1	0
35 RPPA_Clustering_Consensus	0	0	0	1	0

Analyses  
Performed



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<a href="#">COADREAD</a>	29	100%	<a href="#">Open</a> <a href="#">Protected</a>
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### Analysis Overview for Ovarian Serous Cystadenocarcinoma

Maintained by [TCGA GDAC Team](#) (Broad Institute/Dana-Farber Cancer Institute/Harvard Medical School)

- Overview
- Introduction
- Summary

**Note:** These results are offered to the community as an additional reference point, enabling a wide range of cancer biologists, clinical investigators, and genome and computational scientists to easily incorporate TCGA into the backdrop of ongoing research. While every effort is made to ensure that Firehose input data and algorithms are of the highest possible quality, these analyses have not been reviewed by domain experts.

- Results
  - Sequence and Copy Number Analyses
    - Copy number analysis (GISTIC2)  
[View Report](#) | There were 547 tumor samples used in this analysis: 29 significant arm-level results, 35 significant focal amplifications, and 46 significant focal deletions were found.
    - Mutation Analysis (MutSig)  
[View Report](#) | Significantly mutated genes ( $q \leq 0.1$ ): 24
  - Clustering Analyses
    - Clustering of mRNA expression: consensus NMF  
[View Report](#) | The most robust consensus NMF clustering of 565 samples using the 1500 most variable genes was identified for  $k = 3$  clusters. We computed the clustering for  $k = 2$  to  $k = 8$  and used the cophenetic correlation coefficient to determine the best solution.
    - Clustering of mRNA expression: consensus hierarchical  
[View Report](#) | The 1500 most variable genes were selected. Consensus average linkage hierarchical clustering of 565 samples and 1500 genes identified 3 subtypes with the stability of the clustering increasing for  $k = 2$  to  $k = 8$  and the average silhouette width calculation for selecting the robust clusters.
    - Clustering of Methylation: consensus NMF  
[View Report](#) | The 1229 most variable methylated genes were selected based on variation. The variation cutoff are set for each tumor type empirically by fitting a bimodal distribution. For genes with multiple methylation probes, we chose the most variable one to represent the gene. Consensus NMF clustering of 551 samples and 1229 genes identified 6 subtypes with the stability of the clustering increasing for  $k = 2$  to  $k = 8$  and the average silhouette width calculation for selecting the robust clusters.
    - Clustering of miR expression: consensus NMF  
[View Report](#) | We filtered the data to 150 most variable miRs. Consensus NMF clustering of 564 samples and 150 miRs identified 3 subtypes with the stability of the clustering increasing for  $k = 2$  to  $k = 8$  and the average silhouette width calculation for selecting the robust clusters.

View: [Analysis reports](#) [Release notes](#) [FAQ](#) Download: [firehose\\_get](#)

# Organized like a paper

- Overview (“Abstract”)
- Results
- Methods & Data

## With Browser Convenience

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### Analysis Overview for Ovarian Serous Cystadenocarcinoma

Maintained by TCGA, GDC, Team (Broad Institute/Dana-Farber Cancer Institute/Harvard Medical School)

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    - Clustering of Methylation: consensus NMF**  
[View Report](#) | The 1229 most variable methylated genes were selected based on variation. The variation cutoff are set for each tumor type empirically by fitting a bimodal distribution. For genes with multiple methylation probes, we chose the most variable one to represent the gene. Consensus NMF clustering of 557 samples and 1229 genes identified 6 subtypes with the stability of the clustering increasing for  $k = 2$  to  $k = 8$  and the average silhouette width calculation for selecting the robust clusters.
    - Clustering of miR expression: consensus NMF**  
[View Report](#) | We filtered the data to 150 most variable miRs. Consensus NMF clustering of 564 samples and 150 miRs identified 3 subtypes with the stability of the clustering increasing for  $k = 2$  to  $k = 8$  and the average silhouette width calculation for selecting the robust clusters.



# Organized like a paper

- Overview (“Abstract”)
- Results
- Methods & Data

# With Browser Convenience

**Analysis Overview for Ovarian Serous Cystadenocarcinoma**  
Maintained by TCGA, GDHC Team (Broad Institute/Dana-Farber Cancer Institute/Harvard Medical School)

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View Report | The 1500 most variable genes were selected. Consensus average linkage hierarchical clustering of 565 samples and 1500 genes identified 3 subtypes with the stability of the clustering increasing for  $k = 2$  to  $k = 8$  and the average silhouette width calculation for selecting the robust clusters.
    - Clustering of Methylation: consensus NMF  
View Report | The 1229 most variable methylated genes were selected based on variation. The variation cutoff are set for each tumor type empirically by fitting a bimodal distribution. For genes with multiple methylation probes, we chose the most variable one to represent the gene. Consensus NMF clustering of 557 samples and 1229 genes identified 6 subtypes with the stability of the clustering increasing for  $k = 2$  to  $k = 8$  and the average silhouette width calculation for selecting the robust clusters.
    - Clustering of miR expression: consensus NMF  
View Report | We filtered the data to 150 most variable miRs. Consensus NMF clustering of 564 samples and 150 miRs identified 3 subtypes with the stability of the clustering increasing for  $k = 2$  to  $k = 8$  and the average silhouette width calculation for selecting the robust clusters.

## Ovarian Serous Cystadenocarcinoma: Copy number analysis (GISTIC2)

Maintained by Dan DiCara (Broad Institute)

### Overview

#### Introduction

#### Summary

There were 547 tumor samples used in this analysis: 29 significant arm-level results, 35 significant focal amplifications, and 46 significant focal deletions were found.

### Results

#### Focal results

Figure 1. Genomic positions of amplified regions: the X-axis represents the normalized amplification signals (top) and significance by Q value (bottom). The green line represents the significance cutoff at Q value=0.25.

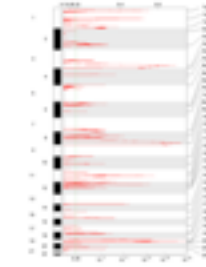


Table 1. Amplifications Table - 35 significant amplifications found. Click the link in the last column to view a comprehensive list of candidate genes. If no genes were identified within the peak, the nearest gene appears in brackets.

Cytoband	Q value	Residual Q value	Wide Peak Boundaries	# Genes in Wide Peak
8q24.21	2.645e-77	2.645e-77	chr8:128574848-129810279	5
19q12	1.8147e-87	8.4949e-76	chr19:34947990-35023082	1
3q26.2	1.0722e-60	1.0722e-60	chr3:170903217-170923258	0 [MECOM]

## Ovarian Serous Cystadenocarcinoma: Clustering of mRNA expression: consensus NMF

Maintained by Robert Zapko (Broad Institute)

### Overview

#### Introduction

#### Summary

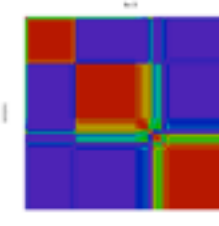
The most robust consensus NMF clustering of 565 samples using the 1500 most variable genes was identified for  $k = 3$  clusters. We computed the clustering for  $k = 2$  to  $k = 8$  and used the cophenetic correlation coefficient to determine the best solution.

### Results

#### Gene expression patterns of molecular subtypes

#### Consensus and correlation matrix

Figure 2. The consensus matrix after clustering shows 3 clusters with limited overlap between clusters.



# Organized like a paper

- Overview (“Abstract”)
- Results
- Methods & Data

# With Browser Convenience

**Analysis Overview for Ovarian Serous Cystadenocarcinoma**  
Maintained by TCGA, GDHC Team (Broad Institute/Dana-Farber Cancer Institute/Harvard Medical School)

- Overview
- Introduction
- Summary
- Note: These results are offered to the community as an additional reference point, enabling a wide range of cancer biologists, clinical investigators, and genome and computational scientists to easily incorporate TCGA into the backdrop of ongoing research. While every effort is made to ensure that Firehose input data and algorithms are of the highest possible quality, these analyses have not been reviewed by domain experts.
- Results
  - Sequence and Copy Number Analyses
    - Copy number analysis (GISTIC2)**  
View Report | There were 547 tumor samples used in this analysis: 29 significant arm-level results, 35 significant focal amplifications, and 46 significant focal deletions were found.
    - Mutation Analysis (MutSig)**  
View Report | Significantly mutated genes ( $q \leq 0.1$ ): 24
  - Clustering Analyses
    - Clustering of mRNA expression: consensus NMF**  
View Report | The most robust consensus NMF clustering of 565 samples using the 1500 most variable genes was identified for  $k = 3$  clusters. We computed the clustering for  $k = 2$  to  $k = 8$  and used the cophenetic correlation coefficient to determine the best solution.
    - Clustering of mRNA expression: consensus hierarchical**  
View Report | The 1500 most variable genes were selected. Consensus average linkage hierarchical clustering of 565 samples and 1500 genes identified 3 subtypes with the stability of the clustering increasing for  $k = 2$  to  $k = 8$  and the average silhouette width calculation for selecting the robust clusters.
    - Clustering of Methylation: consensus NMF**  
View Report | The 1229 most variable methylated genes were selected based on variation. The variation cutoff are set for each tumor type empirically by fitting a bimodal distribution. For genes with multiple methylation probes, we chose the most variable one to represent the gene. Consensus NMF clustering of 557 samples and 1229 genes identified 6 subtypes with the stability of the clustering increasing for  $k = 2$  to  $k = 8$  and the average silhouette width calculation for selecting the robust clusters.
    - Clustering of miR expression: consensus NMF**  
View Report | We filtered the data to 150 most variable miRs. Consensus NMF clustering of 564 samples and 150 miRs identified 3 subtypes with the stability of the clustering increasing for  $k = 2$  to  $k = 8$  and the average silhouette width calculation for selecting the robust clusters.

## Ovarian Serous Cystadenocarcinoma: Copy number analysis (GISTIC2)

Maintained by Dan DiCara (Broad Institute)

### Overview

#### Introduction

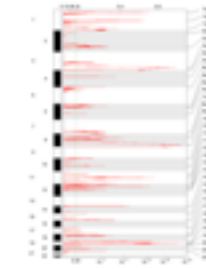
#### Summary

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### Results

#### Focal results

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## Ovarian Serous Cystadenocarcinoma: Clustering of mRNA expression: consensus NMF

Maintained by Robert Zapko (Broad Institute)

### Overview

#### Introduction

#### Summary

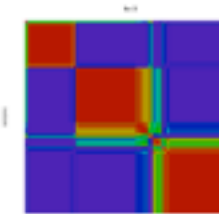
The most robust consensus NMF clustering of 565 samples using the 1500 most variable genes was identified for  $k = 3$  clusters. We computed the clustering for  $k = 2$  to  $k = 8$  and used the cophenetic correlation coefficient to determine the best solution.

### Results

#### Gene expression patterns of molecular subtypes

#### Consensus and correlation matrix

**Figure 2.** The consensus matrix after clustering shows 3 clusters with limited overlap between clusters.



Completely Open: no passwords  
Linked to downloadable data

## - Summary

There were 558 tumor samples used in this analysis: 29 significant arm-level results, 34 significant focal amplifications, and 47 significant focal deletions were found.

## - Results ●

### + Focal results ●

### - Arm-level results ●

GET FULL TABLE

**Table 3.** Arm-level significance table - 29 significant results found.

Arm	# Genes	Amp Frequency	Amp Z score	Amp Q value	Del Frequency	Del Z score	Del Q value
1p	2121	0.21	0.131	1	0.10	-5.72	1
1q	1955	0.34	6.49	4.26e-10	0.09	-6.29	1
2p	924	0.27	-2.25	1	0.07	-10.7	1
2q	1556	0.22	-2.32	1	0.07	-9.07	1
3p	1062	0.23	-3.6	1	0.20	-4.8	1
3q	1139	0.49	9.71	0			
4p	489	0.14	-7.22	1			
4q	1049	0.07	-7.69	1			

- Standard visual format for ALL pipelines



## - Summary

There were 558 tumor samples used in this analysis: 29 significant arm-level results, 34 significant focal amplifications, and 47 significant focal deletions were found.

## - Results ●

### + Focal results ●

### - Arm-level results ●

GET FULL TABLE

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- Standard visual format for ALL pipelines
- As little as 3-5 simple R calls
- Thoughtfully Scoped:
  - drill from overview to details
  - Significant results “bubble up”

## - Summary

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## - Results ●

### + Focal results ●

### - Arm-level results ●

GET FULL TABLE

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There were 558 tumor samples used in this analysis: 29 significant arm-level results, 34 significant focal amplifications, and 47 significant focal deletions were found.

## - Results ●

### + Focal results ●

### - Arm-level results ●

GET FULL TABLE

RIGOR: nothing thrown away

Table 3. Arm-level significance table - 29 significant results found.

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# Firehose Reports | At-a-Glance



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**Download Results**  
This is an experimental feature. The full results of the analysis summarized in this report can be downloaded from the TCGA Data Coordination Center.

- Analysis Results (MD5 checksum)
- Auxiliary Data (MD5 checksum)
- MAGE-TAB File (MD5 checksum)

**References**

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Again, aimed at solid design & engineering

Nozzle package downloadable as open source

Used in multiple external projects

# Programmatic, Too

---

```
firehose_get : retrieve open-access results of Broad Institute TCGA GDAC runs
Version: 0.3.3 (Author: Michael S. Noble)

Usage: firehose_get [flags] RunType Date [tumor_type, ... ]
```

# firehose\_get

```
BLCA BRCA CESC COADREAD DLBC GBM HNSC KIRC KIRP LAML LGG LIHC
LNNH LUAD LUSC OV PAAD PRAD SKCM STAD THCA UCEC PANCANCER
```

- Download all or parts
- Of data or analyses runs
- **Open access : no password**
- Select by run type & date
- Subselect by tumor type
- Or analyses type / name
- See what runs we did
- Or what tasks in each run

**10K download from [gdac.broadinstitute.org](http://gdac.broadinstitute.org)**

```
% firehose_get -runs
```

Run	At_DCC	Available_From_Broad_GDAC
...		
analyses__2012_04_25	yes	yes
analyses__2012_05_25	yes	yes
analyses__2012_06_23	yes	yes
analyses__2012_07_25	no	yes

```
% firehose_get -tasks analyses 2012_07_25
```

```
...  
CopyNumber_Gistic2  
Correlate_Clinical_vs_CopyNumber_Arm  
Correlate_Clinical_vs_Molecular_Signatures  
Correlate_Clinical_vs_Mutation  
...  
Correlate_CopyNumber_vs_miR  
Correlate_CopyNumber_vs_mRNAseq  
Correlate_Methylation_vs_mRNA  
...  
Methylation_Clustering_CNMF  
miRseq_Clustering_CNMF  
miRseq_Clustering_Consensus  
miR_Clustering_CNMF  
...  
mRNAseq_Clustering_CNMF  
...  
mRNAseq_Clustering_Consensus  
mRNAseq_Preprocess  
Mutation_Significance  
...  
Pathway_FindEnrichedGenes  
Pathway_Paradigm_Expression  
...  
RPPA_Clustering_CNMF  
...
```

These analyses are what is described by the reports on our GDAC dashboards



# THANK YOU!

<http://gdac.broadinstitute.org>

[gdac@broadinstitute.org](mailto:gdac@broadinstitute.org)