# **Broad GDAC**

Lung Adenocarcinoma AWG Run 2013\_02\_07

Dan DiCara Hailei Zhang Michael Noble







## **GDAC Firehose Runs**

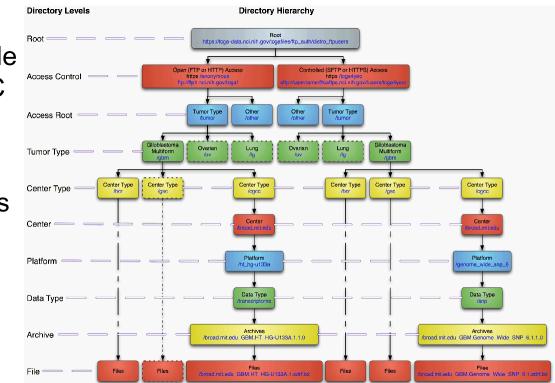
- Firehose was conceived for the purpose of running a suite of analyses automatically on a monthly basis for public consumption and archival storage
- Evolved to include data standardization runs
  - Facilitates running automated analyses on a monthly basis with limited manual intervention
- Recent evolution to support AWGs directly
  - Running all Firehose/GDAC machinery on AWG data freezes and disease subtypes
  - Encapsulate results in browsable biologist friendly reports
  - Simplify data retrieval via firehose\_get

## Outline

- GDAC Overview
  - Nightly mirroring and dicing
  - Workflows (Standard Data & Analyses)
  - Dashboards
  - Biologist Friendly Nozzle Reports
- Lung Adenocarcinoma AWG Run
  - Data freeze
  - Data retrieval via firehose\_get
  - Analyses Results

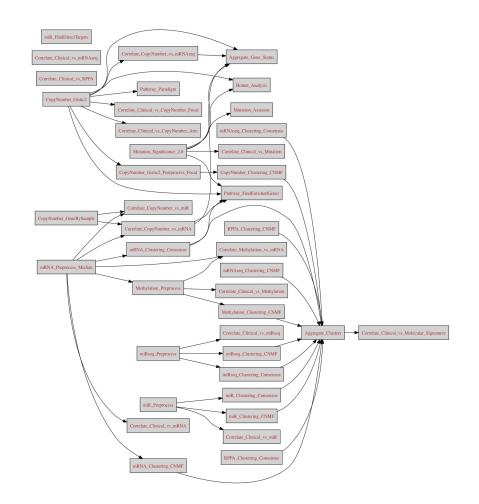
## Nightly Mirroring and Dicing

- Mirroring
  - Maintain an up-to-date snapshot of all available TCGA data at the DCC
- Dicing
  - Standardize data formatting to ensure it's amenable for automated analyses
  - Perform filtering
    - Redactions
    - Blacklisting
    - Replicate filtering



# Workflows (Standard Data & Analyses)

- Standard data
  - 84 data merger pipelines
  - SDRFs generated to document data provenance
- Analyses
  - 41 analysis pipelines
    - Clustering
    - Correlation
    - Mutation
    - Copy number
    - Pathway
  - Biologist friendly result reports included



### **Dashboards**







S9 Added by Aaron Ball, last edited by Michael Noble on Dec 07, 2012 (view change) show comment

- AWG Reps
- AWG Support
- Contact Us
- Dashboard-Analyses
- Dashboard-Stddata
- Data Usage Policy
- DCC Interactions
- Download
- FAQ
- Internal
- Nomenclature
- Nozzle
- Pipeline Docs
- Presentations
- ProcessFlow
- QualityControl
- Run Reports
- TAP
  - Email Archive

#### Tracking System



Welcome to the online home of the Broad Institute's Genome Data Analysis Center (GDAC). On behalf of The Cancer Genome Atlas (TCGA), we've designed and operate scientific data and analysis pipelines which pump terabyte-scale genomic datasets through scores of quantitative algorithms, in the hope of accelerating the understanding of cancer. See the dashboards below for details of the latest monthly runs, or this presentation for more background information. Note that downloading data from our site constitutes agreement to this data usage policy. Monthly Analysis Results

#### Ri-monthly Standard Data Results

	2013_01_16	stddata Run			2012_12_21 analyses Run			
DiseaseType	# Datasets	% Processed	Do	wnload	AnalysisReport	# Pipelines	% Successful	Do
BLCA	78	100%	Open	Protected	BLCA	47	100%	Open
BRCA	117	100%	Open	Protected	BRCA	63	100%	Open
CESC	61	100%	Open	Protected	CESC	44	100%	Open
COADREAD	93	100%	Open	Protected	COADREAD	63	100%	Open
COAD	91	100%	Open	Protected	COAD	63	100%	Open
DLBC	25	100%	Open	Protected	GBM	65	100%	Open
GBM	119	100%	Open	Protected	HNSC	47	100%	Open
HNSC	83	100%	Open	Protected	KICH	24	100%	Open
KICH	43	100%	Open	Protected	KIRC	63	100%	Open
KIRC	88	100%	Open	Protected	KIRP	60	100%	Open
KIRP	81	100%	Open		LGG	60	100%	Open
LAML	28	100%	Open	Protected	LIHC	16	100%	Open
LGG	58	100%	Open	Protected	LUAD	63	100%	Open
LIHC	66	100%		Protected	LUSC	63	100%	Open
LUAD	104	100%	Open		OV	69	100%	Open
LUSC	112	100%	Open	Protected	PAAD	21	100%	Open
OV	153	100%	Open		PRAD	44	100%	Open
PAAD	48	100%	Open		READ	63	100%	Open
PRAD	62	100%	Open		SARC	11	100%	Open
READ	93	100%			SKCM	47	100%	Open
SARC	40	100%	Open		STAD	42	100%	Open
SKCM	75	100%	Open	Protected	THCA	94	100%	Open
STAD	58	100%	Open		UCEC	63	100%	Open
THCA	97	100%	Open	Protected	LAML	12	<u>92%</u>	Open
UCEC	93	100%			DLBC	6	86%	Open
PANCAN12	230	94%	Open	Protected	PANCAN12	6	38%	Open

View analysis reports or click on dashboards above or download with firehose get.

November 2012 Firehose runs were not done, read here to understand why



🖉 Edit 🖂 Share 🕂 Add 🗸 🌼 Tools 🗸

Added by Michael Noble, last edited by Michael Noble on Jan 18, 2013 (view change)

See this presentation on the role of Firehose within The Cancer Genome Atlas, and note that downloading data from our site constitutes agreement to this data usage policy.

	Sample Counts Table	201	2_12_21 a	nalyses I	Run	Sam	ples Summary Report	t
Prior Analysis Runs		Tables of Ingested D	ata: HTML PNG	TSV Sampl	es Summa	ry: Report		
Oct 24, 2012		Tublet et ingested b		<u>tor</u> oump	oo oanna			
		AnalysisReport	# Pipelines	% Successfu	I Dow	nload		
Sept 13, 2012		BLCA	47	<u>100%</u>		Protected		
Aug 25, 2012		BRCA	63	<u>100%</u>		Protected		
-		CESC COADREAD	44 63	<u>100%</u> 100%		Protected Protected		
July 25, 2012		COAD	63	100%		Protected		
June 23, 2012		GBM	65	100%		Protected		
50110 20, 2012	Analysis Reports	HNSC	47	100%			Download Data	
May 25, 2012		KICH	24	100%		Protected	2 Connota Data	
		KIRC	63	<u>100%</u>	Open	Protected		
April 25, 2012		KIRP	60	<u>100%</u>		Protected		
March 21, 2012		LGG	60	<u>100%</u>		Protected		
		HC	16	100%		Protected		
Feb 17, 2012		LUAD LUSC	63 63	<u>100%</u> 100%		Protected		
lan 04, 0040		OV	69	100%		Protected Protected		
<u>Jan 24, 2012</u>		PAAD	21	100%		Protected		
Dec 30, 2011		PRAD	44	100%		Protected		
		READ	63	100%		Protected		
Nov 28, 2011		SARC	11	100%		Protected		
Oct 26, 2011		SKCM	47	100%	Open	Protected		
001 28, 2011		STAD	42	100%	Open	Protected		
Sept 21, 2011		THCA	94	<u>100%</u>		Protected		
		UCEC	63	<u>100%</u>		Protected		
July 28, 2011		LAML	12	<u>92%</u>		Protected		
May 25, 2011		DLBC PANCAN12	6 6	<u>86%</u> 38%		Protected Protected		
May 20, 2011		PANCAN12 PANCAN18	4	<u>38%</u> 31%		Protected Protected		
April 21, 2011		PAROANIO	-7	0176		TOLOGICU		
March 27, 2011								
Feb 17, 2011	Vi	iew: <u>Analysis reports</u>	Release notes	<u>FAQ</u>	Download	firehose_	<u>get</u>	



#### Summary of TCGA Tumor Data Ingested into Broad GDAC Pipeline 2013\_02\_03 stddata Run

Tumor	BCR	Clinical	CN	LowP	Methylation	mRNA	mRNAseq	miR	miRseq	RPPA	MAF
BLCA	153	117	152	105	153	0	122	0	135	54	28
BRCA	929	869	899	0	888	527	841	0	894	408	507
CESC	134	32	114	0	122	0	97	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	18	0	17	0	0	0	16	0	0
ESCA	20	0	0	0	20	0	0	0	0	0	0
GBM	598	565	563	0	405	542	161	491	0	214	291
HNSC	358	318	322	108	310	0	303	0	326	212	306
KICH	66	0	66	0	65	0	66	0	66	0	0
KIRC	502	502	493	0	500	72	480	0	481	454	293
KIRP	159	103	117	0	103	16	76	0	117	0	100
LAML	202	200	197	0	194	0	179	0	187	0	199
LGG	222	208	220	0	176	27	174	0	221	0	170
LIHC	99	62	97	0	98	0	34	0	96	0	0
LUAD	508	333	403	0	430	32	353	0	401	237	229
LUSC	399	327	358	0	359	154	258	0	349	195	178
OV	592	580	566	0	584	574	297	570	454	412	316
PAAD	57	0	57	0	49	0	31	0	34	0	34
PANCAN12	5345	4853	5021	423	4905	2179	3415	1061	4264	2785	2819
PRAD	190	148	177	0	172	0	140	0	177	0	83
READ	169	168	162	35	162	69	72	0	143	130	69
SARC	52	0	29	0	29	0	0	0	29	0	0
SKCM	288	184	273	119	288	0	265	0	272	164	253
STAD	308	162	237	0	257	0	43	0	237	0	116
THCA	500	287	430	94	435	0	379	0	411	224	323
UCEC	512	451	493	106	500	54	370	0	487	200	248
Totals	7468	6039	6856	636	6736	2222	4933	1061	6062	3173	3934

	EXPAND ALL COLLAPSE ALL SET AUTO WIDTH PRINT	
S	tddata2013_02_03 Samples Summary Report	
-	Overview	U
-	Introduction	- 11
	The Broad GDAC mirrors data from the DCC on a daily basis. Although all data is mirrored, not every samples is ingested into Firehose. There are three main mechanisms that filter samples to ensure that only the most scientifically relevant samples make it into our standard data and analyses runs. These three mechanisms are redactions, replicate filtering, and blacklisting. This report summarizes the data that is ingested into Firehose. It describes the three filtering mechanisms and lists those samples that are removed.	
+	Summary	
-	Results	
+	Redactions	
+	Replicate Filtered Samples	- 11
+	Blacklisted Samples	- 11
-	Sample Heatmaps	- 11
	BLCA	- 11
	GET HIGH-RES IMAGE Figure 1. This figure depicts the distribution of available data on a per participant basis.	





**Dashboard-Analyses** 

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Added by Michael Noble, last edited by Michael Noble on Jan 18, 2013 (view change)

See this presentation on the role of Firehose within The Cancer Genome Atlas, and note that downloading data from our site constitutes agreement to this data usage policy.

	Sample Counts Table	201	2_12_21 a	analyses F	Run	San	nples Summary Report
Prior Analysis Runs						Deere	
Oct 04, 0010	1	Tables of Ingested Da	ata: <u>HIML PNC</u>	sample	es Summ	ary: <u>Repor</u>	1
<u>Oct 24, 2012</u>		AnalysisReport	# Pipelines	% Successful	l Do	wnload	
Sept 13, 2012		BLCA	47	100%	Open	Protected	
Aug 05, 0040		BRCA	63	<u>100%</u>	Open	Protected	
Aug 25, 2012		CESC	44	<u>100%</u>	<u>Open</u>	Protected	
July 25, 2012		COADREAD	63	<u>100%</u>	<u>Open</u>	Protected	
		COAD	63	100%	<u>Open</u>	Protected	
<u>June 23, 2012</u>	Analysis Departs	GBM	65	100%	<u>Open</u>	Protected	
May 05, 0040	Analysis Reports	HNSC	47	100%	Open Open		Download Data
May 25, 2012		KICH	24 63	<u>100%</u> 100%	Open Open	Protected	
April 25, 2012		KIRC KIRP	60	100%	Open Open	Protected Protected	
<u></u>			60	100%	Open	Protected	
March 21, 2012		AIHC	16	100%		Protected	
E 1 47 0040		LUAD	63	100%	Open	Protected	
Feb 17, 2012		LUSC	63	100%	Open	Protected	
Jan 24, 2012		OV	69	100%	Open	Protected	
		PAAD	21	100%	Open	Protected	
Dec 30, 2011		PRAD	44	100%	Open	Protected	
		READ	63	100%	Open	Protected	
Nov 28, 2011		SARC	11	100%	Open	Protected	
Oct 26, 2011		SKCM	47	<u>100%</u>	<u>Open</u>	Protected	
00120, 2011		STAD	42	<u>100%</u>	<u>Open</u>	Protected	
Sept 21, 2011		THCA	94	<u>100%</u>	<u>Open</u>	Protected	
		UCEC	63	<u>100%</u>	<u>Open</u>	Protected	
<u>July 28, 2011</u>		LAML	12	<u>92%</u>	<u>Open</u>	Protected	
May 25, 2011		DLBC	6	86%	Open	Protected	
Way 20, 2011		PANCAN12	6	38%	Open	Protected	
April 21, 2011		PANCAN18	4	<u>31%</u>	<u>Open</u>	Protected	
March 27, 2011							
Feb 17, 2011	Vie	ew: Analysis reports	Release note	<u>s FAQ</u> I	Downloa	d: <u>firehose</u>	get

### **Biologist Friendly Nozzle Reports**

#### Analysis Overview for Lung Adenocarcinoma

Maintained by TCGA GDAC Team (Broad Institute/MD Anderson Cancer Center/Harvard Medical School)

#### Overview

#### Introduction

This is the analysis overview for Firehose run "21 December 2012".

#### 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 356 tumor samples used in this analysis: 27 significant arm-level results, 30 significant focal amplifications, and 45 significant focal deletions were found.

    Mutation Analysis (MutSig v2.0)
  - View Report
  - Mutation Analysis (MutSig vS2N)
  - View Report
- Clustering Analyses
  - Clustering of copy number data: consensus NMF

<u>View Report</u> | The most robust consensus NMF clustering of 356 samples using the 75 copy number focal regions 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 Methylation: consensus NMF

<u>View Report</u> | The 3800 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 304 samples and 3800 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 RPPA data: consensus NMF

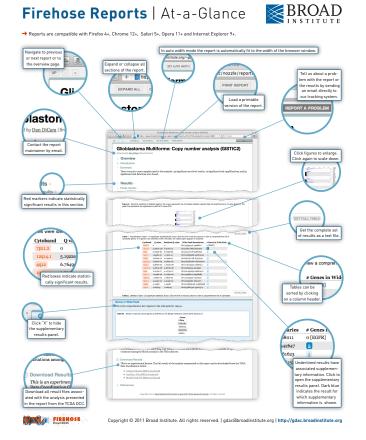
<u>View Report</u> | The most robust consensus NMF clustering of 237 samples using the 150 most variable proteins was identified for k = 3 clusters. We computed the clustering for k = 2 to k = 8 and used the cophenetic correlation coefficient to determine the best solution.

• Clustering of RPPA data: consensus hierarchical

<u>View Report</u> | The 150 most variable proteins were selected. Consensus average linkage hierarchical clustering of 237 samples and 150 proteins identified 4 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 mRNA expression: consensus NMF

# Biologist Friendly Nozzle Reports cont.'d



Maintained by <u>Dan DiCara</u> (B					alysis (GISTIC2)	
Overview						
+ Introduction						
- Summary						
There were 356 tum 45 significant focal d			s analysis: 27 sigi	nificant arm-level results	, 30 significant focal amplifications, a	and
- Results •						
<ul> <li>Focal results</li> </ul>						
Figure 1. Genomic po (bottom). The green lin	sitions of amp ne represents t	plified regions he significanc	: the X-axis represent e cutoff at Q value=0.	s the normalized amplification 25.	signals (top) and significance by Q value	
Figure 1. Genomic po (bottom). The green lir	sitions of amp	plified regions.	the X-axis represent	s the normalized amplification	signals (top) and significance by Q value	
(bottom). The green lin	is Table - 30 s	ignificant am	e cutoff at Q value=0.		GET FULL YAB	LE
(bottom). The green lin	is Table - 30 s	ignificant am	e cutoff at Q value=0.	25.	GET FULL YAB	LE
(bottom). The green lin	ns Table - 30 s genes were id Cytoband 14q13.3	ignificant am ntified within	e cutoff at Q value=0.	25.	o view a comprehensive list of # Genes in Wide Peak	LE
(bottom). The green lin	ns Table - 30 s genes were idd Cytoband 14413-3 8q24-21	ignificant am entified within Q value 4.4377e-43 9.2147e-19	e cutoff at Q value=0.	25.	o view a comprehensive list of # Genes in Wide Peak 2	LE
(bottom). The green lin	ns Table - 30 s genes were id Cytoband 14q13.3	ignificant am entified within Q value 4.4377°-43	e cutoff at Q value=0.	25.	o view a comprehensive list of # Genes in Wide Peak	LE

### Data Freeze

- Standard data and analyses runs performed on a frozen subset of samples
- Subtype analyses possible (i.e. run the entire GDAC pipeline on each subtype)
  - Molecular Smoker
  - Molecular Non-smoker
  - Oncogene Positive

#### — ...

### Analysis Overview for 07 February 2013

Maintained by TCGA GDAC Team (Broad Institute/MD Anderson Cancer Center/Harvard Medical School)

#### Unique Tumor Sample Counts

Tumor	BCR	Clinical	CN	Methylation	mRNA	mRNASeq	miRSeq	RPPA	MAF
luad	230	229	230	229	23	230	230	181	129
				load run result	s with <u>fire</u>				

Simplest download command: firehose\_get awg\_luad 2013\_02\_07

For More Help: firehose\_get --help

Overview

+ Introduction

**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.

A total of 199 reports are available for analysis run "07 February 2013".

Results

#### Cancer Types

Table 1. Click "Browse" to view reports for a cancer type of interest. If you prefer to view reports on your own computer, you may download a ZIP archive containing all reports for a cancer type by clicking "Download".

Cancer Type	Cohort	Reports	HTML	ZIP
Lung Adenocarcinoma	LUAD-BRONCHIOID	26	Browse	Download
Lung Adenocarcinoma	LUAD-MAGNOID	30	Browse	Download
Lung Adenocarcinoma	LUAD-MOLECULAR_NONSMOKER	30	Browse	Download
Lung Adenocarcinoma	LUAD-MOLECULAR_SMOKER	31	Browse	Download
Lung Adenocarcinoma	LUAD-ONCOGENE_NEGATIVE	26	Browse	Download
Lung Adenocarcinoma	LUAD-ONCOGENE_POSITIVE	30	Browse	Download
Lung Adenocarcinoma	LUAD-SQUAMOID	26	Browse	Download

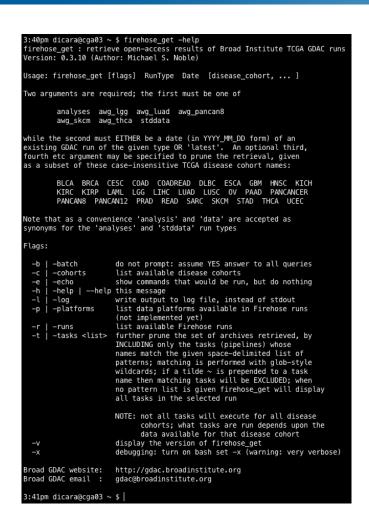
An archive containing all reports for the 07 February 2013 run is available for <u>download</u>. Links to archives with reports for individual cancer types are included in Table 1.

http://gdac.broadinstitute.org/runs/awg\_luad\_2013\_02\_07/reports

Summary

## Data Retrieval via firehose\_get

- Central location for collaborators to retrieve data and analyses for an AWG freeze
  - Easy data retrieval: firehose\_get awg\_luad 2013\_02\_07
  - Ensures consistency across all centers analyzing TCGA data for an AWG
  - Easier than passing around a freeze list and having each analyst curate his/her own frozen data



### **Analyses Results Outline**

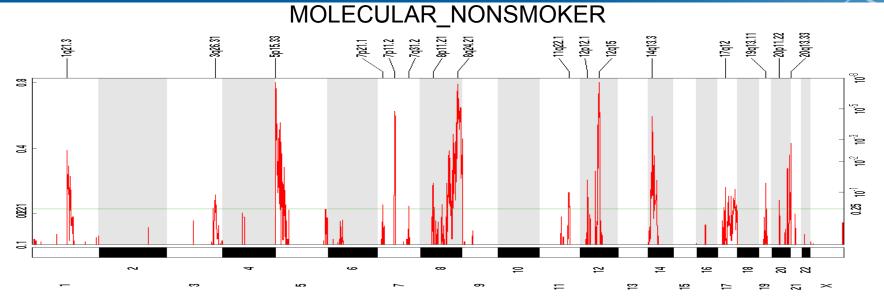
SubtypesNo. patientsMolecular\_Nonsmoker81Molecular\_Smoker149Oncogene\_Negative96Oncogene\_Positive134Bronchioid89Magnoid63Squamoid78

The analysis include copy number GISTIC, Mutsig (v2.0 & s2N), clustering for expression platforms, Integrated with clinical info, Pathway analysis– Hotnet and

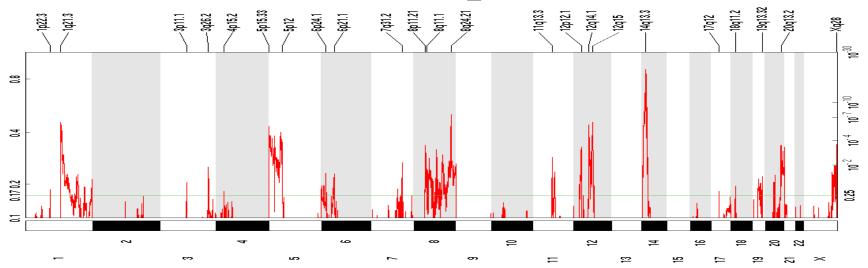
# IGV view of copy number -- Nonsmokers and smokers



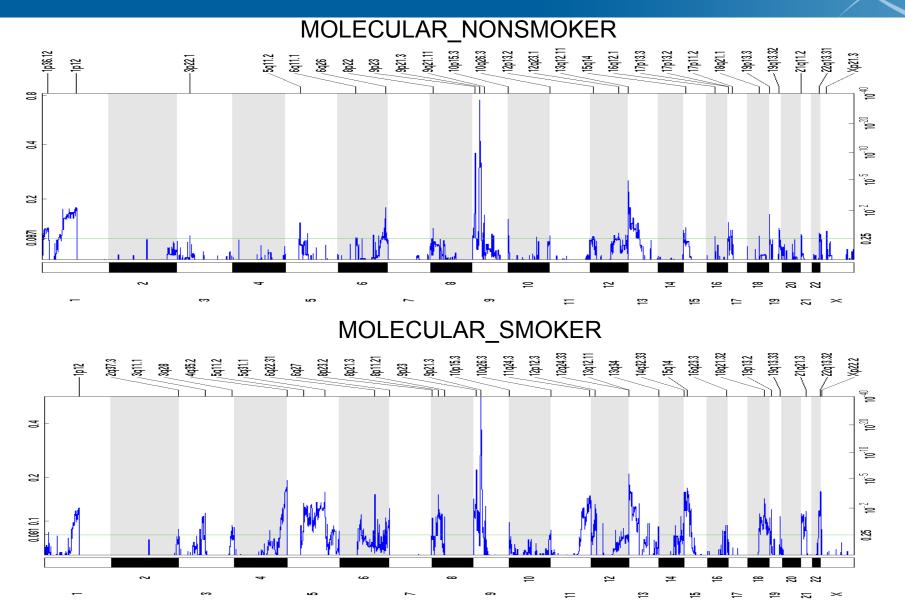
### Copy number analysis (GISTIC 2) – Focal Amplifications



MOLECULAR\_SMOKER



# Copy number analysis (GISTIC 2) – Focal Deletions



### Nonsmoker--MutSig 2.0 and S2N

Μ	utsig S2N		I	Mutsig v2.	0
gene	р	q	gene	р	q
TP53	0	0	TP53	1.1e-14	2e-10
SETD2	5.9e-32	5.6e-28	EGFR	1e-11	9.1e-08
EGFR	1.7e-27	1.1e-23		<b>E</b> ( ) 00	
BRAF	1.8e-22	8.4e-19	CDKN2A	5.4e-08	0.00033
EIF5B	3.3e-19	1.2e-15	SMAD4	1.6e-07	0.00072
CDKN2 A	5.9e-17	1.8e-13	KRAS	3.7e-07	0.0013
SMAD4	2.9e-10	7.8e-07	KEAP1	5.9e-07	0.0018
KEAP1	6.3e-10	1.5e-06	CSMD3	1e-06	0.0027
	4 0 00	0.00002	BRAF	0.000018	0.041
GLG1	1.3e-08	8	SPTA1	0.000034	0.063
KRAS	3.5e-06	0.0065	STK11	0.000035	0.063
LONP1	0.00001 6	0.028	OR4A5	0.000055	0.09

\* No mutation genes are correlated with clinical info.

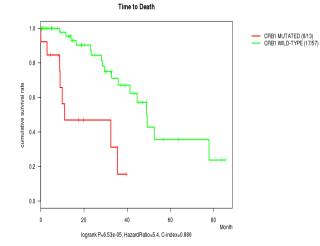
### Smoker--MutSig 2.0 and S2N

Mutsig S2N

gene	р	q
TP53	2.9e-82	5.6e-78
KRAS	1.1e-47	1.1e-43
STK11	2.9e-35	1.8e-31
RBM10	3.2e-30	1.5e-26
FAM75C1	4e-21	1.5e-17
ZNF770	6.4e-12	2e-08
AGAP6	1.9e-08	0.000051
ZNF679	2.7e-08	0.000064
FSCB	2.3e-07	0.00047
HRNR	3.5e-06	0.0067
KEAP1	8.9e-06	0.015

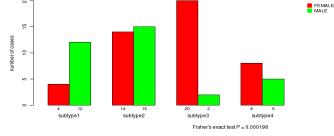
Mutsig v2.0 – top 10

gene	р	q	
KRAS		2.78E-15	2.71E-11
TP53		4.55E-15	2.71E-11
KEAP1		5.77E-15	2.71E-11
STK11		6.00E-15	2.71E-11
REG3A		9.02E-10	3.26E-06
NAV3		8.56E-09	2.58E-05
SNTG1		2.06E-08	4.84E-05
SLITRK2		2.14E-08	4.84E-05
OR2T33		2.44E-08	4.90E-05
RIMS2		2.83E-08	5.12E-05
CD5L		4.31E-08	7.08E-05
	С	RB1	



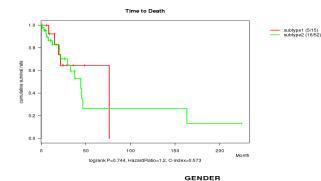
### Nonsmoker--mRNAseq gene expression clustering

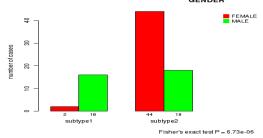
#### **cNMF** Time to Death 1.0 subtype1 (3/13) subtype2 (12/25) subtype3 (6/18) subtype4 (0/11) 0.8 rate 0.6 survival 0.4 0.2 0.0 0 50 100 150 200 Month lograph P - 0.00799 GENDER - 5

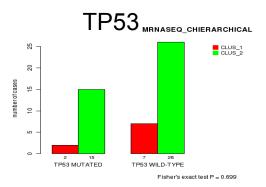


<figure><figure><figure><figure><figure>

### cHierarchical

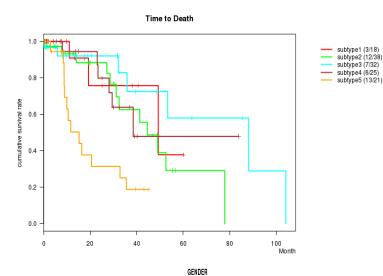


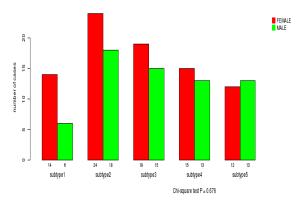




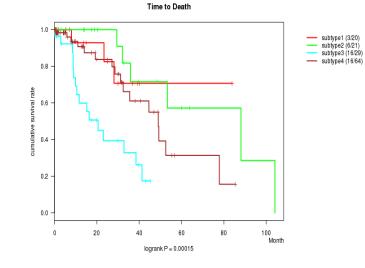
### Smoker --- mRNAseq gene expression clustering

### **cNMF**

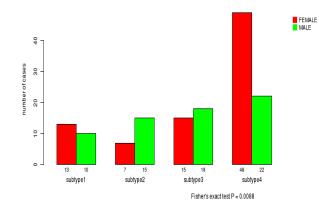




### **cHierarchical**



GENDER



# PARADIGM pathway analysis of mRNASeq expression and copy number data

### MOLECULAR\_NONSMOKER

Pathway.Name	Avg.Num.Perturbations
IL4-mediated signaling events	11
FOXA2 and FOXA3 transcription factor networks	11
Signaling events mediated by the Hedgehog family	9
Signaling mediated by p38-alpha and p38-beta	9
Syndecan-4-mediated signaling events	7
Osteopontin-mediated events	6
HIF-1-alpha transcription factor network	6
Endothelins	6
EGFR-dependent Endothelin signaling events	6
Nephrin/Neph1 signaling in the kidney podocyte	5

### MOLECULAR\_SMOKER

Pathway.Name	Avg.Num.Perturbations
Signaling events mediated by the Hedgehog family	20
IL4-mediated signaling events	20
Signaling mediated by p38-alpha and p38-beta	18
Endothelins	16
HIF-1-alpha transcription factor network	14
FOXA2 and FOXA3 transcription factor networks	14
Syndecan-1-mediated signaling events	13
Wnt signaling	13
IL23-mediated signaling events	13
Visual signal transduction: Cones	12