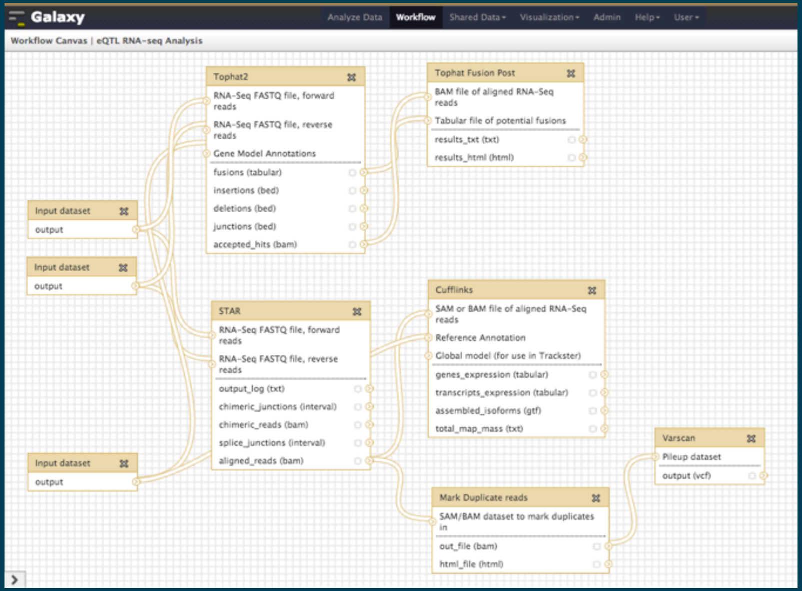
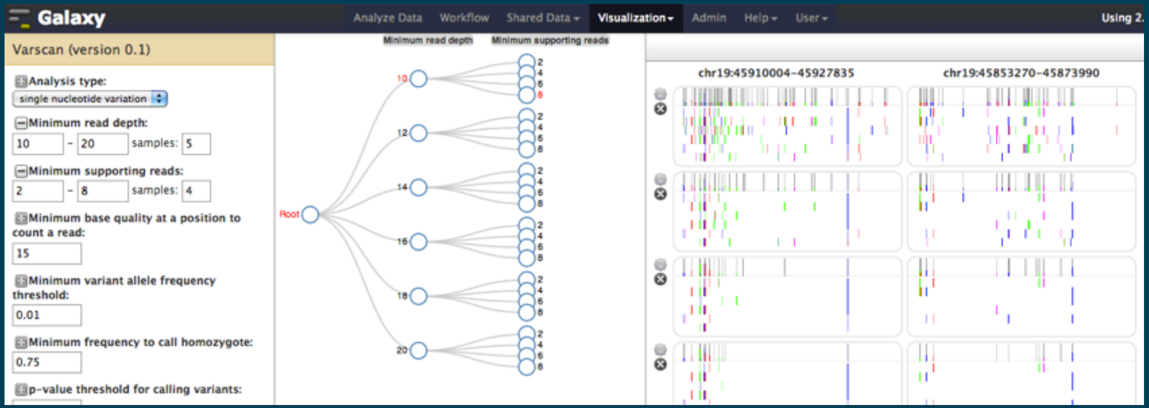




Varscan (version 0.1)

Analysis type: single nucleotide variation

Minimum read depth: 10 - 20 samples: 5

Minimum supporting reads: 2 - 8 samples: 4

Minimum base quality at a position to count a read: 15

Minimum variant allele frequency threshold: 0.01

Minimum frequency to call homozygote: 0.75

p-value threshold for calling variants:

Galaxy

Understanding Cancer Genomes (and Transcriptomes!) using Galaxy

Jeremy Goecks

Department of Biology
Department of Math and Computer Science
Emory University

EMORY
UNIVERSITY

Advancing Computing and Genomics

Research model

1. find computing challenge while doing genomics
2. invent new computing technology to address challenge
3. demonstrate usefulness of new technology via genomics investigation

Advancing Computing and Genomics

Realizing research model

1. computing challenge: analyzing cancer genomes
2. new computing technology: Galaxy tools, workflows, and visual analysis
3. genomics investigation: pancreatic cancer transcriptome

Roadmap

Galaxy

Analyzing Cancer Genomes and Transcriptomes

Vision

Galaxy is an **open, Web-based platform** for accessible, reproducible, and collaborative computational genomics

A User Perspective of Galaxy

GUI for high-throughput, high-performance genomics

1. get and integrate public, private data
2. analyze data and create workflows
3. visualization and visual analysis, sharing, publication

Customizable open-source software on various HPC resources

- public website — http://usegalaxy.org
- local instance
- on the cloud

A Developer Perspective of Galaxy

Module (plug-in) architecture

- {attributes + behaviors} define a module, and module implementations are written as needed

There are Galaxy module definitions/support for:

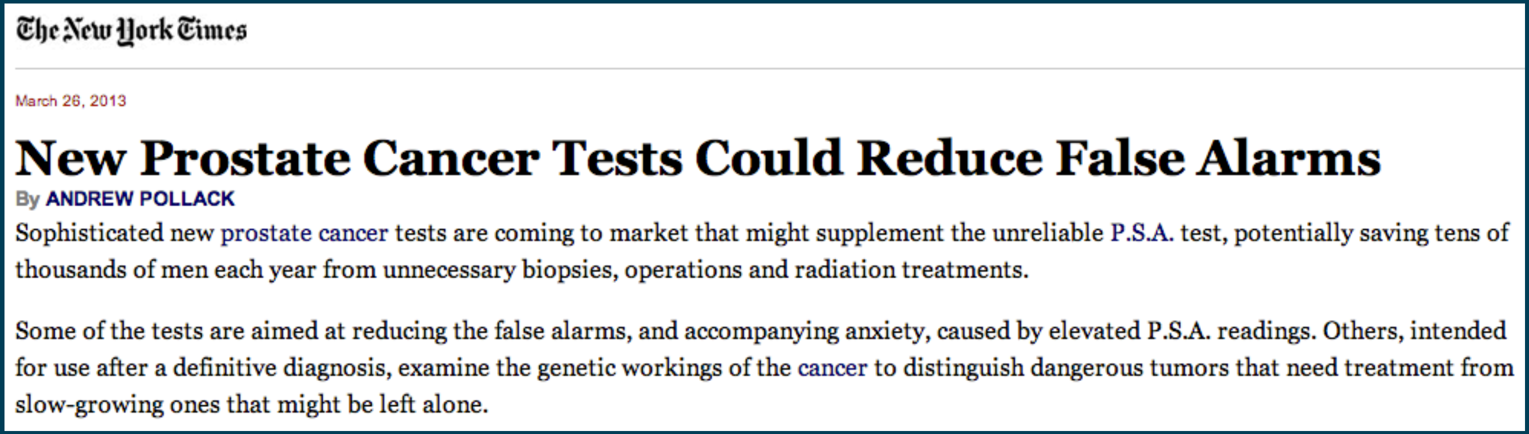
- tools
- data types (file formats)
- data sources (e.g., sequencers)
- data stores (file systems)
- job scheduling engines (e.g., DRMAA, Condor)
- visualizations/visual analysis (e.g., genome browser, Circos plot, scatterplot)

Roadmap

Galaxy

Analyzing Cancer Genomes and Transcriptomes

Cancer Genomics



The New York Times

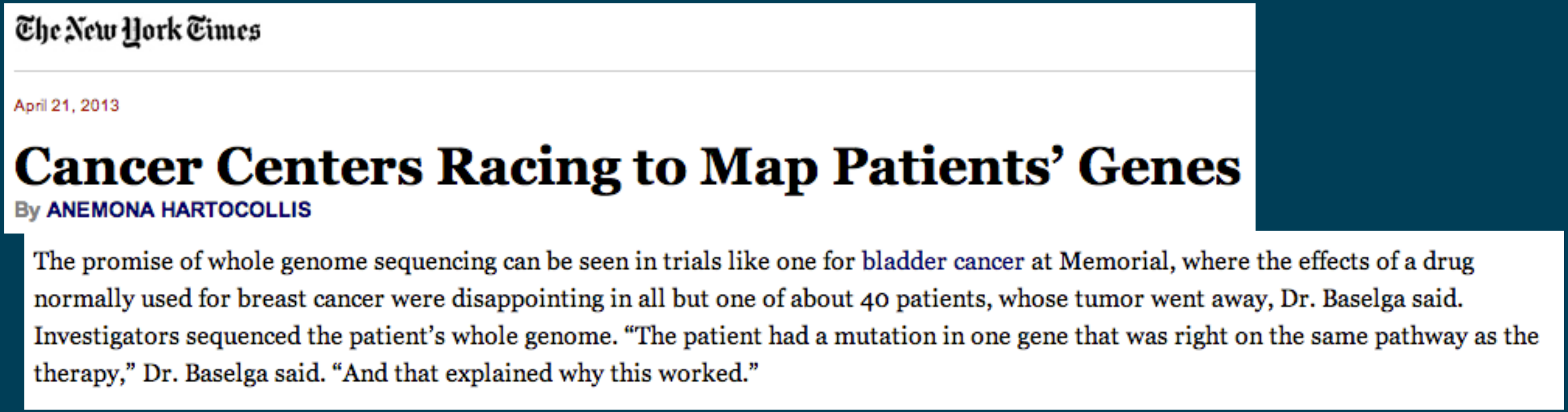
March 26, 2013

New Prostate Cancer Tests Could Reduce False Alarms

By ANDREW POLLACK

Sophisticated new prostate cancer tests are coming to market that might supplement the unreliable P.S.A. test, potentially saving tens of thousands of men each year from unnecessary biopsies, operations and radiation treatments.

Some of the tests are aimed at reducing the false alarms, and accompanying anxiety, caused by elevated P.S.A. readings. Others, intended for use after a definitive diagnosis, examine the genetic workings of the cancer to distinguish dangerous tumors that need treatment from slow-growing ones that might be left alone.



The New York Times

April 21, 2013

Cancer Centers Racing to Map Patients' Genes

By ANEMONA HARTOCOLLIS

The promise of whole genome sequencing can be seen in trials like one for bladder cancer at Memorial, where the effects of a drug normally used for breast cancer were disappointing in all but one of about 40 patients, whose tumor went away, Dr. Baselga said. Investigators sequenced the patient's whole genome. "The patient had a mutation in one gene that was right on the same pathway as the therapy," Dr. Baselga said. "And that explained why this worked."

Using Galaxy for Analysis of Cancer Genomes/Transcriptomes

New tools

- e.g. variant calling, fusion detection, variant annotation and filtering, VCF manipulation

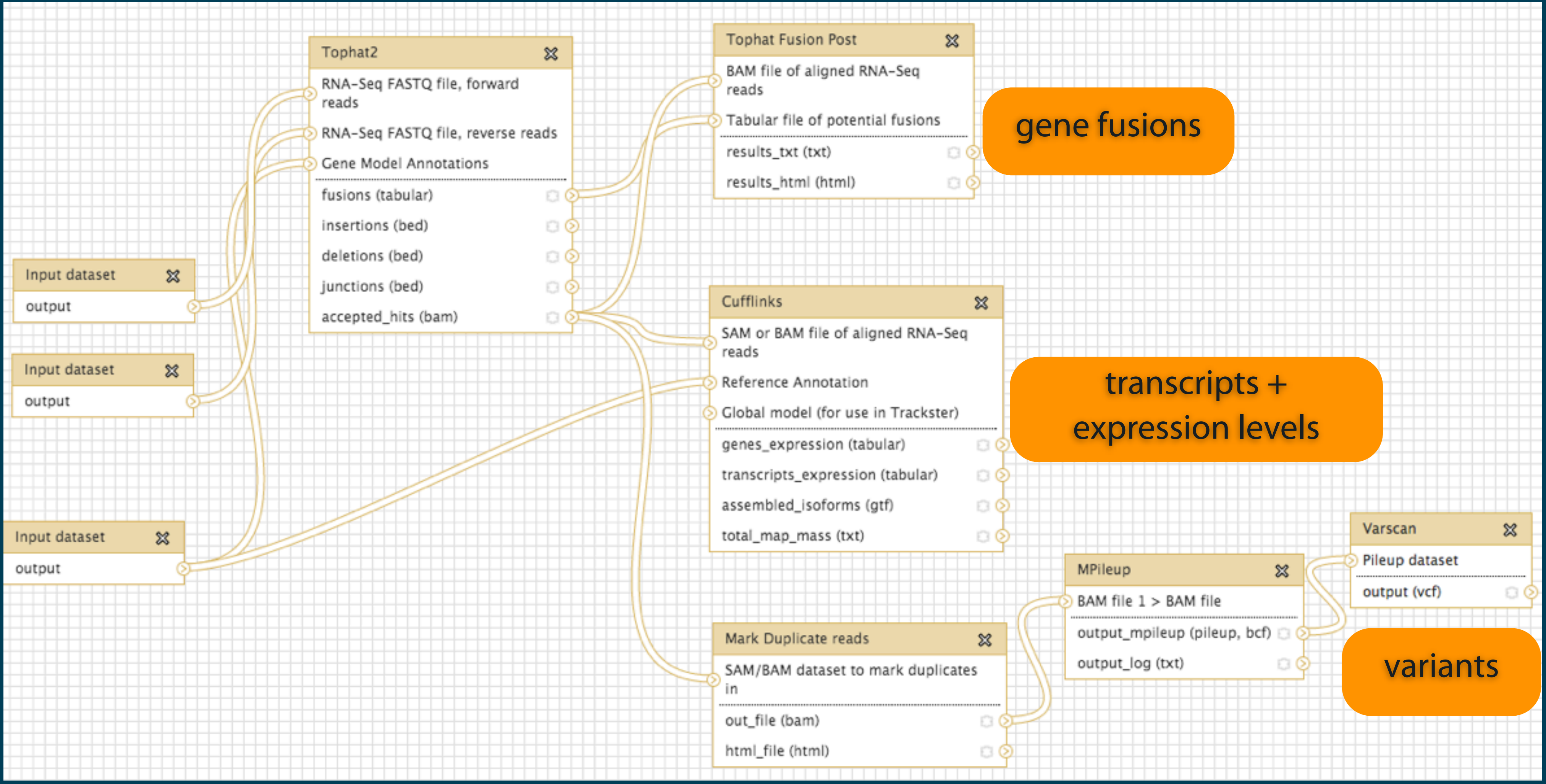
New workflows

- workflows are understandable and extendable

New visual analysis applications

- visualize and call variants in a Web browser

Single Sample Transcriptome Analysis



gene fusions

transcripts + expression levels

variants

Advantages of Galaxy Workflows

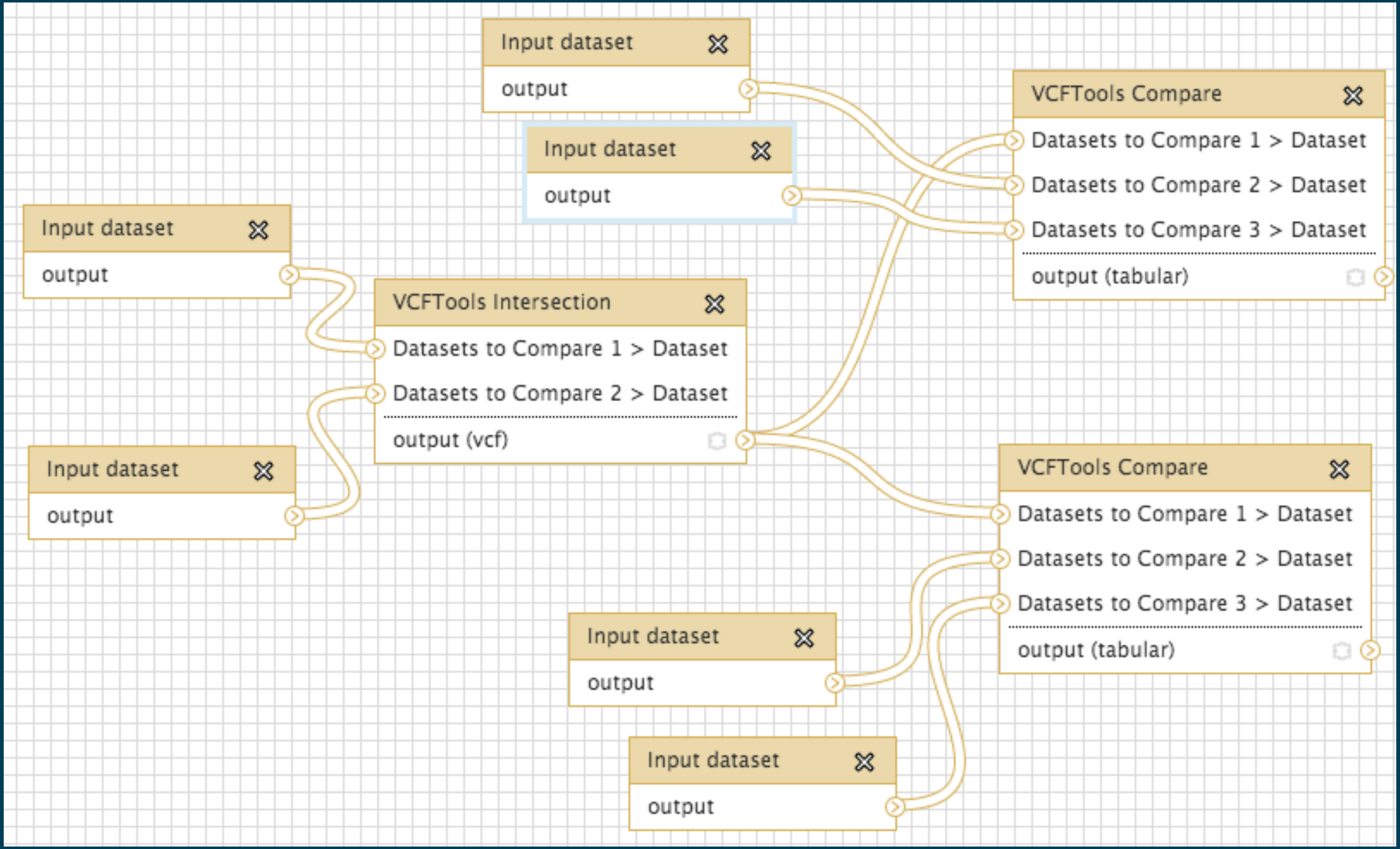
Not a black box, so can swap out tools and modify parameters

- recomputable

Human readable, especially for non-programmers

“-able”: import, export, share, publish, embed

Comparing Called Variants with Public Datasets


Input dataset
output
Input dataset
output
Input dataset
output
Input dataset
output
VCFTools Intersection
Datasets to Compare 1 > Dataset
Datasets to Compare 2 > Dataset
output (vcf)
VCFTools Compare
Datasets to Compare 1 > Dataset
Datasets to Compare 2 > Dataset
Datasets to Compare 3 > Dataset
output (tabular)
VCFTools Compare
Datasets to Compare 1 > Dataset
Datasets to Compare 2 > Dataset
Datasets to Compare 3 > Dataset
output (tabular)
Input dataset
output
Input dataset
output

Patient Mutations vs. CCLE Cancer Cell Line Encyclopedia

http://www.broadinstitute.org/ccle/home

	P1	P2	P3	P4	P5	P6	CL
OM MIA (4)	0	1	1	0	0	0	4
OM PC (11)	0	1	1	0	0	0	4
HP MIA (84)	6	6	5	5	4	4	19
HP PC (1769)	21	29	23	14	29	15	49

Cell line does not appear very similar to tumors

OM = OncoMap, HP = hybrid capture with probes

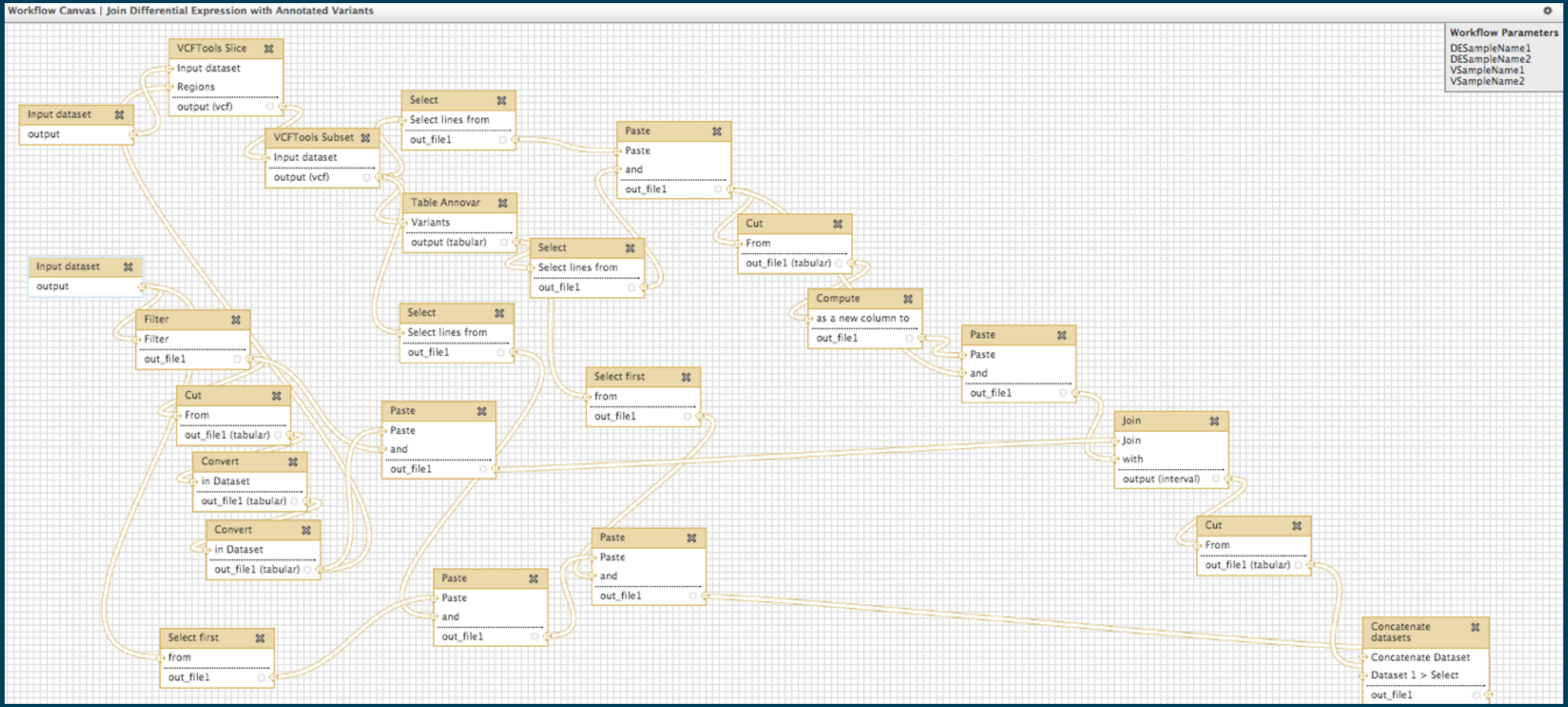
Using Mutations for Characterizing Tumors

	P1	P2	P3	P4	P5	P6
OM MIA (4)	0	1	1	0	0	0
OM PC (11)	0	1	1	0	0	0
HP MIA (84)	6	6	5	5	4	4
HP PC (1769)	21	29	23	14	29	15
Tumor %	90%	90%	100%	0%?	60%	40%

OM = OncoMap, HP = hybrid capture with probes

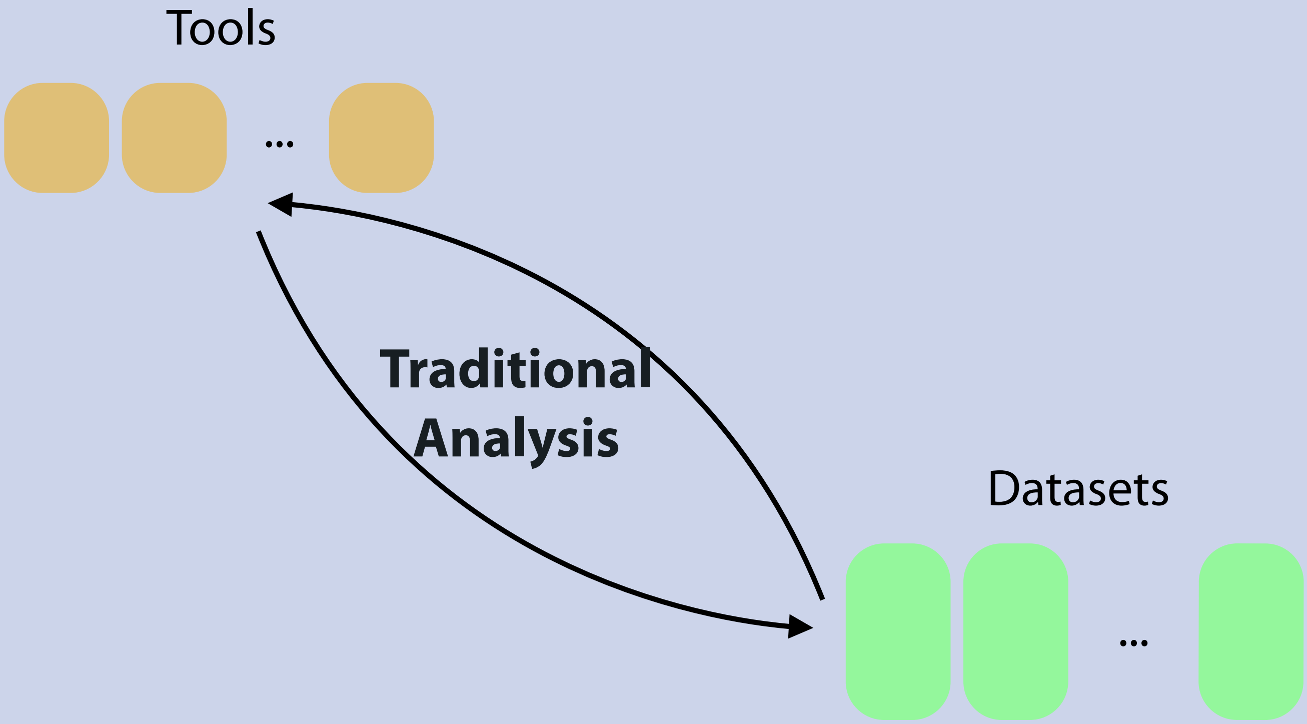
(See ISMB talk for discussion of clustering patients via gene expression data from RNA-seq.)

Variants + Gene Expression + Annotation:
Targeted eQTL Analysis

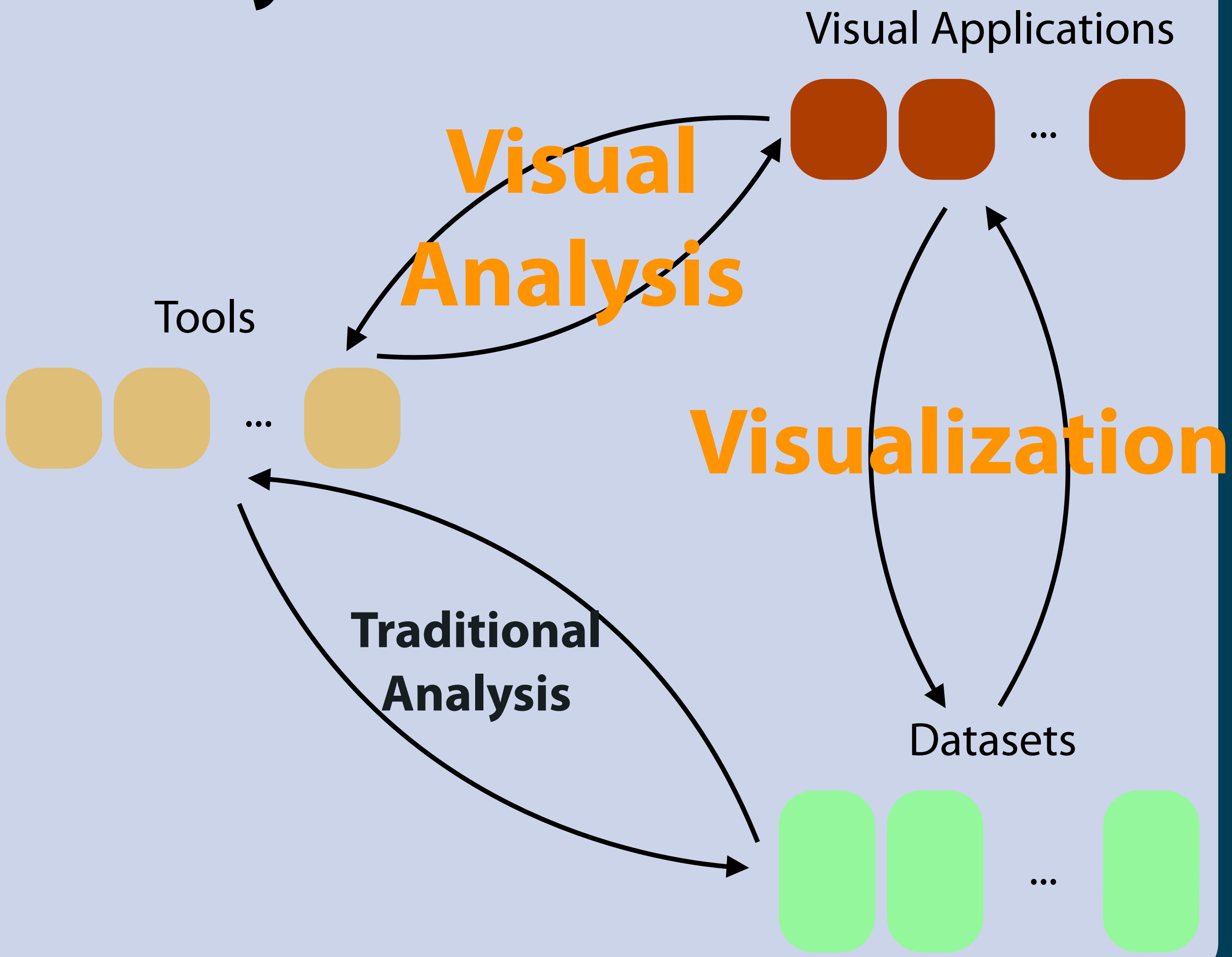


Finds and annotates variants in differentially-expressed genes or isoforms

Galaxy



Galaxy



Visual Applications

Visual Analysis

Tools

Visualization

Traditional Analysis

Datasets

Web-based Visualization for High-throughput Genomic Datasets

State-of-the-art data management

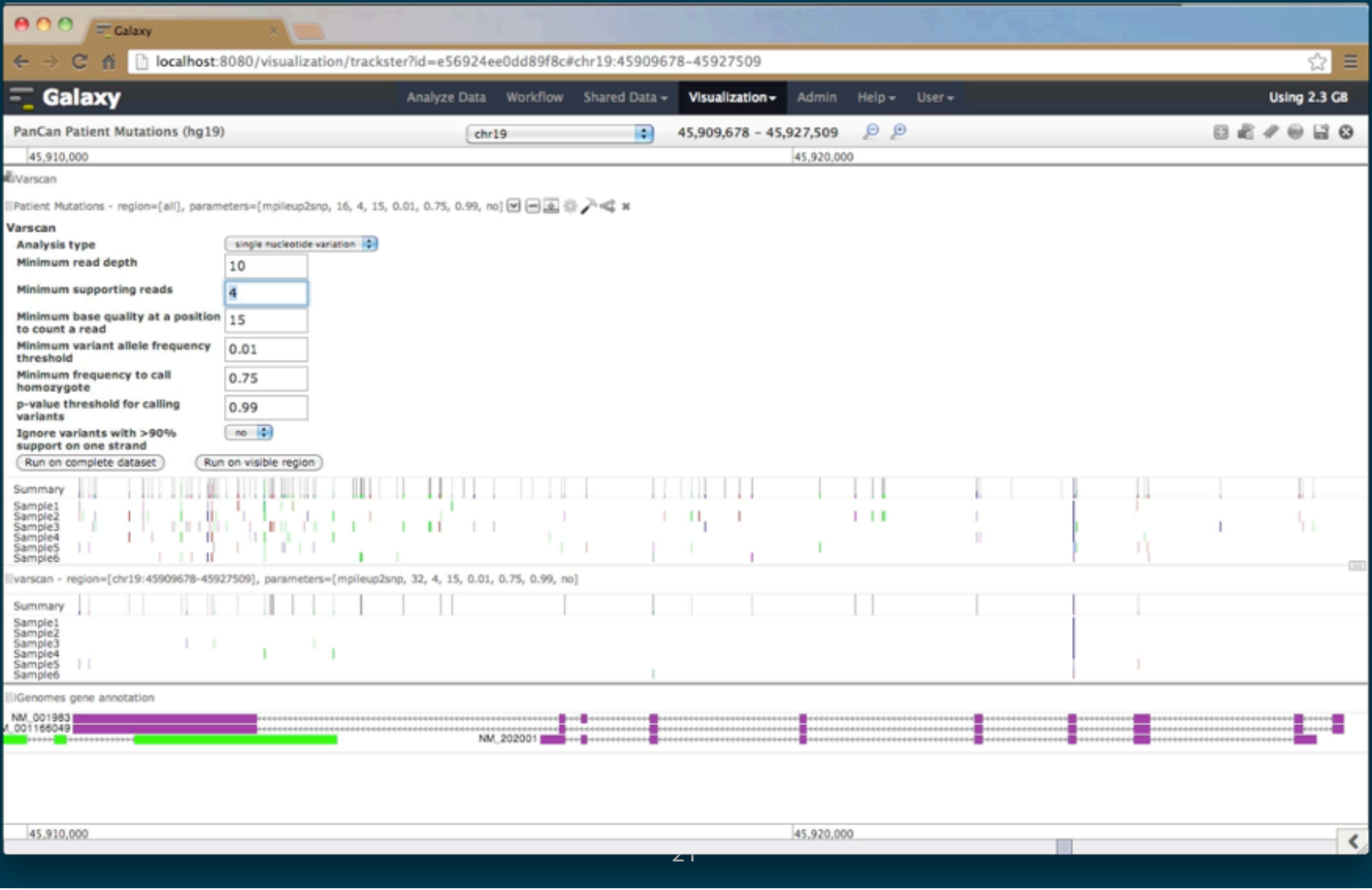
- automatic indexing for aggregate data and individual data points
- data on demand + multi-level caching

Can share and publish fully-functional visualizations

Framework for adding new visualizations

- similar to tool config in Galaxy

Trackster



PanCan Patient Mutations (hg19)

chr19 45,909,678 - 45,927,509

Varscan

Patient Mutations - region=[all], parameters=[mpileup2snp, 16, 4, 15, 0.01, 0.75, 0.99, no]

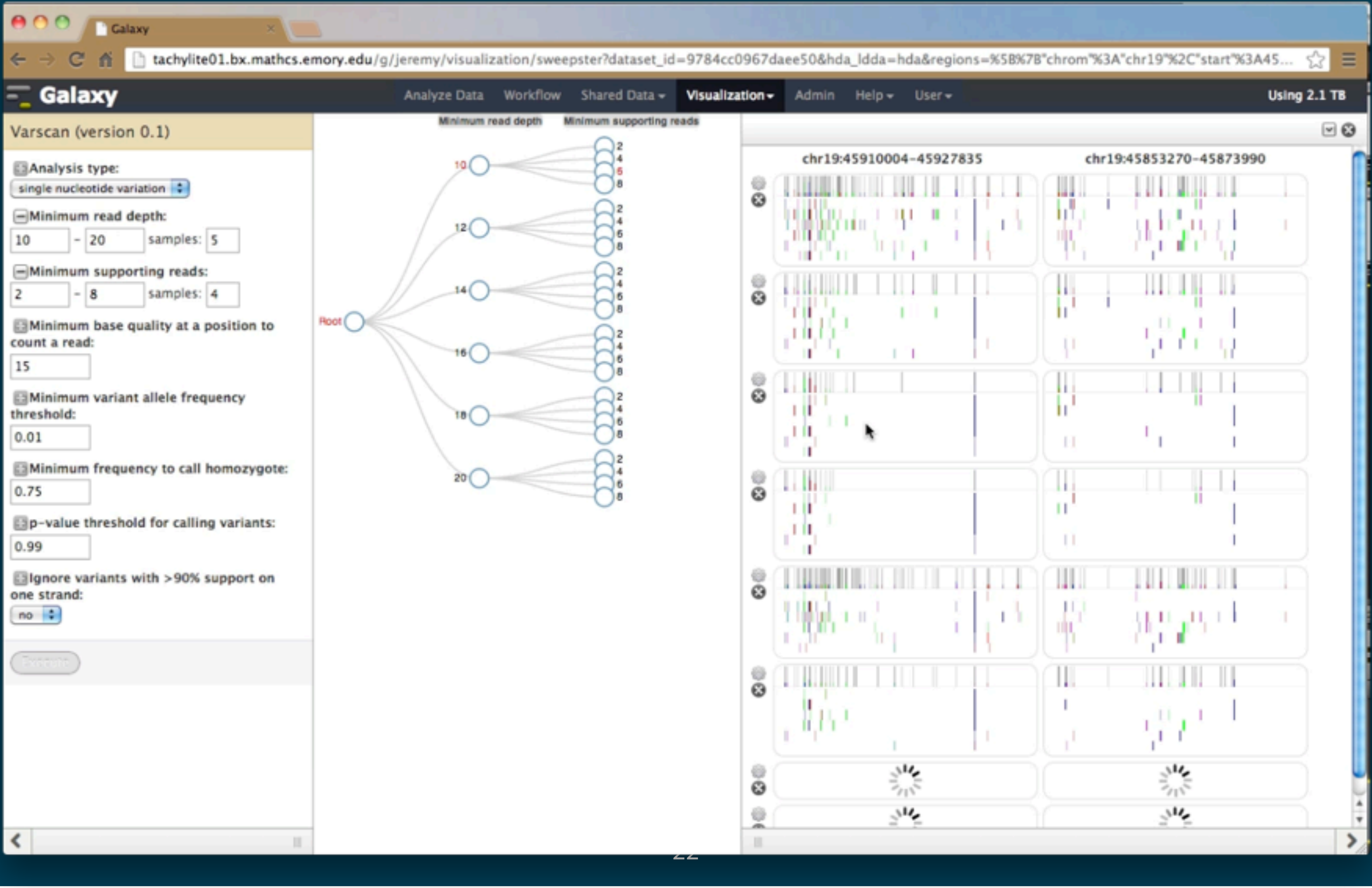
Varscan

Analysis type	single nucleotide variation
Minimum read depth	10
Minimum supporting reads	4
Minimum base quality at a position to count a read	15
Minimum variant allele frequency threshold	0.01
Minimum frequency to call homozygote	0.75
p-value threshold for calling variants	0.99
Ignore variants with >90% support on one strand	no

varscan - region=[chr19:45909678-45927509], parameters=[mpileup2snp, 32, 4, 15, 0.01, 0.75, 0.99, no]

iGenomes gene annotation

Sweepster



Galaxy
tachylite01.bx.mathcs.emory.edu/g/jeremy/visualization/sweepster?dataset_id=9784cc0967daee50&hda_ldda=hda&regions=%5B%7B"chrom"%3A"chr19"%2C"start"%3A45...
Galaxy
Analyze Data
Workflow
Shared Data
Visualization
Admin
Help
User
Using 2.1 TB

Varscan (version 0.1)

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p-value threshold for calling variants: 0.99

Ignore variants with >90% support on one strand: no

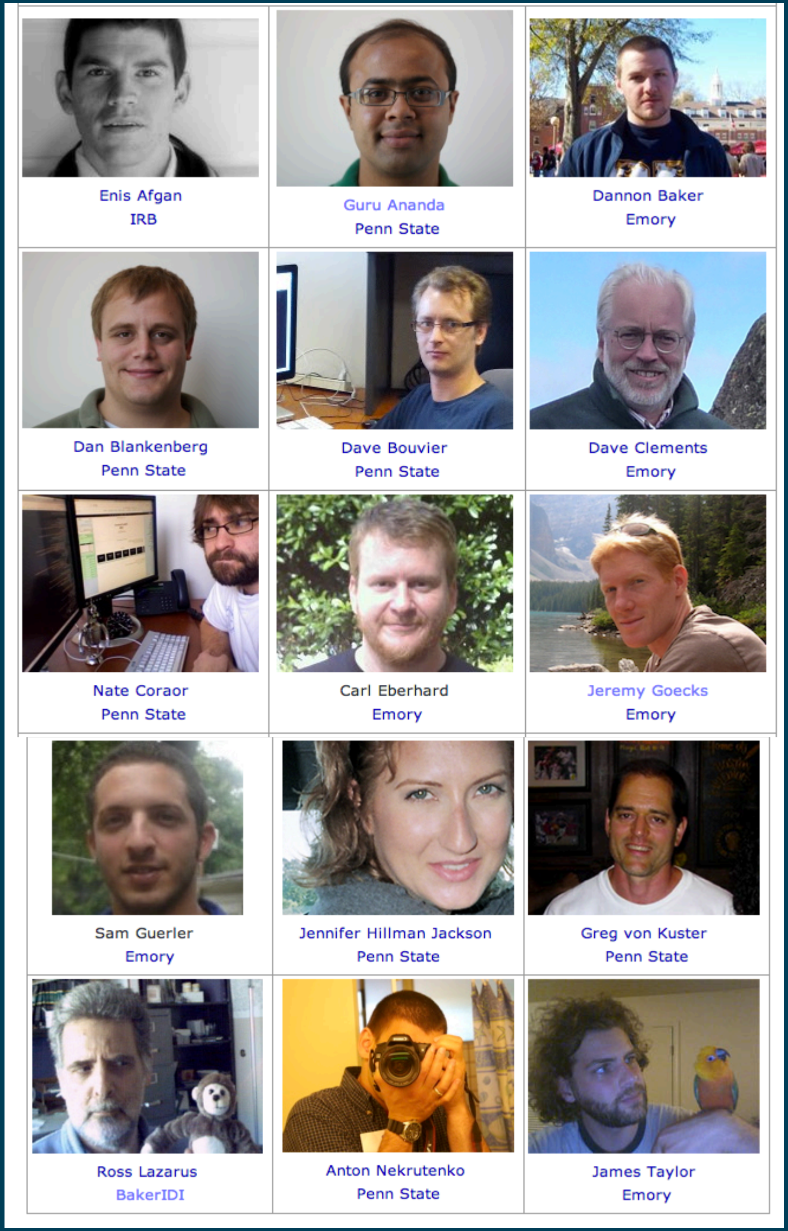
Real-time Visual Analysis

Interactive use of production tool to call and visualize variants for multiple patients using parameter sweeps

A general approach for interactive visual analysis on very large genomics datasets

- any Galaxy visual application, many tools (original application: transcript assembly)
- can decide what data to analyze on the fly
- workflows soon!

Galaxy



Enis Afgan
IRB

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Penn State

Dannon Baker
Emory

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Dave Bouvier
Penn State

Dave Clements
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Nate Coraor
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Jeremy Goecks
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A Cancer Center Designated by
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Mike Rossi

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National Human Genome Research Institute
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NSF
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WHERE DISCOVERIES BEGIN

Thanks! And More:

Galaxy

http://galaxyproject.org
http://usegalaxy.org

http://bitbucket.org/galaxy/galaxy-central
http://wiki.galaxyproject.org

2013
ISMB
ECCB

1 **Longer Talk, more Biology**

Sunday, 14:10-14:35

2 **Integrated Visualization & Computing Workshop**

Tuesday, 14:10-16:05