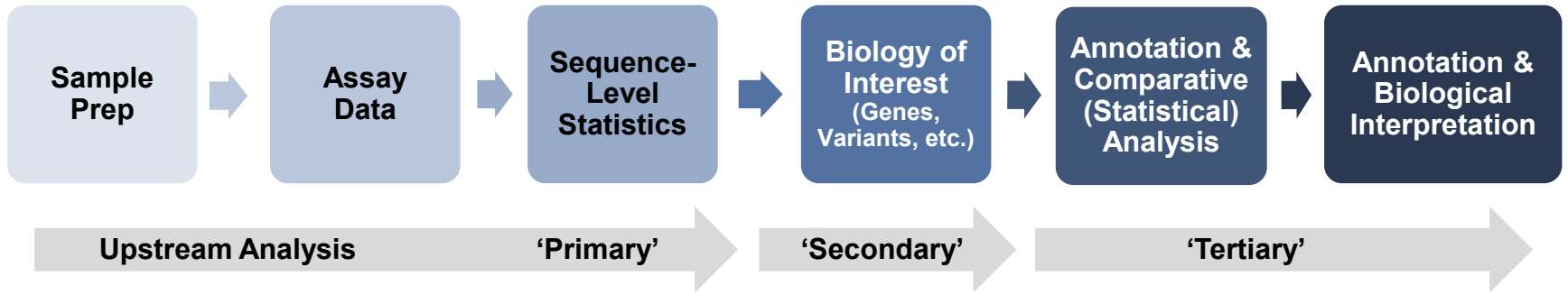


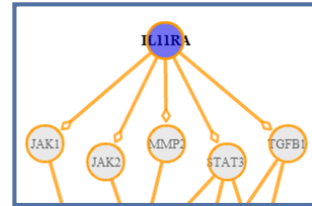
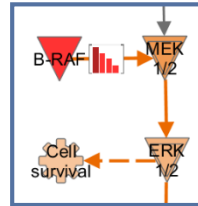
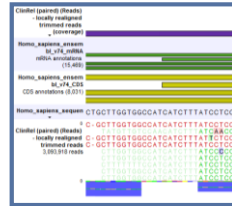
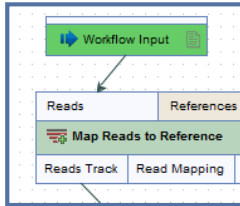
Jennifer Poitras, Ph.D.
Field Applications Scientist
Qiagen Advanced Genomics
Jennifer.Poitras@qiagen.com

CLC Biomedical Genomics Workbench General Overview





Sample



BRAF c.1798_1799del... p.V600K Likely Pathogenic	BRCA1 c.68_69delAG p.E23fs*17
MYBPC3 c.1624G>C p.E542Q Likely Pathogenic	PIK3CA c.3075C>T p.T1025T Benign

Insight

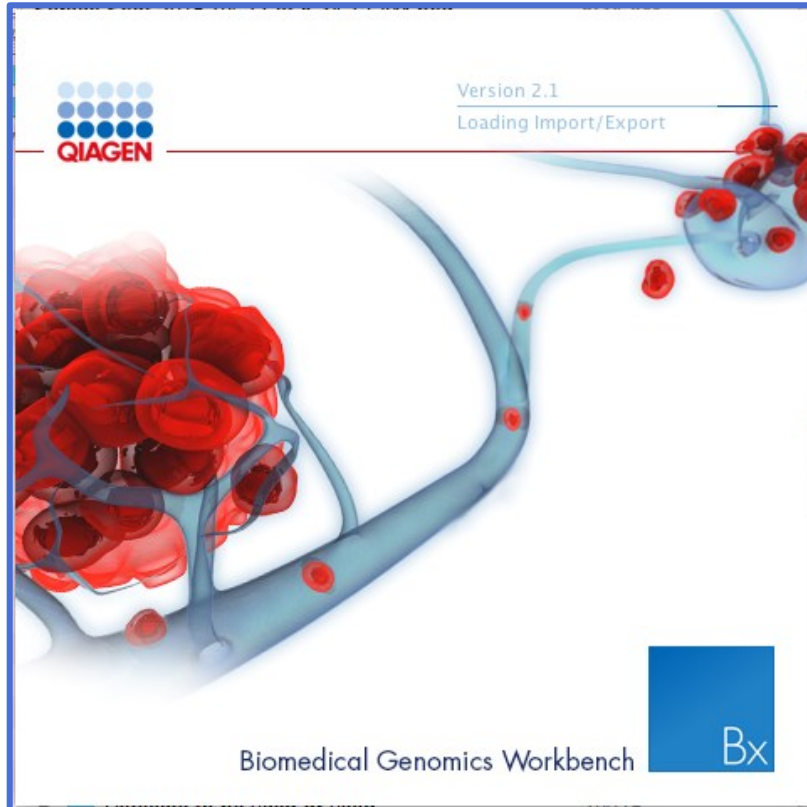


INGENUITY
PATHWAY ANALYSIS

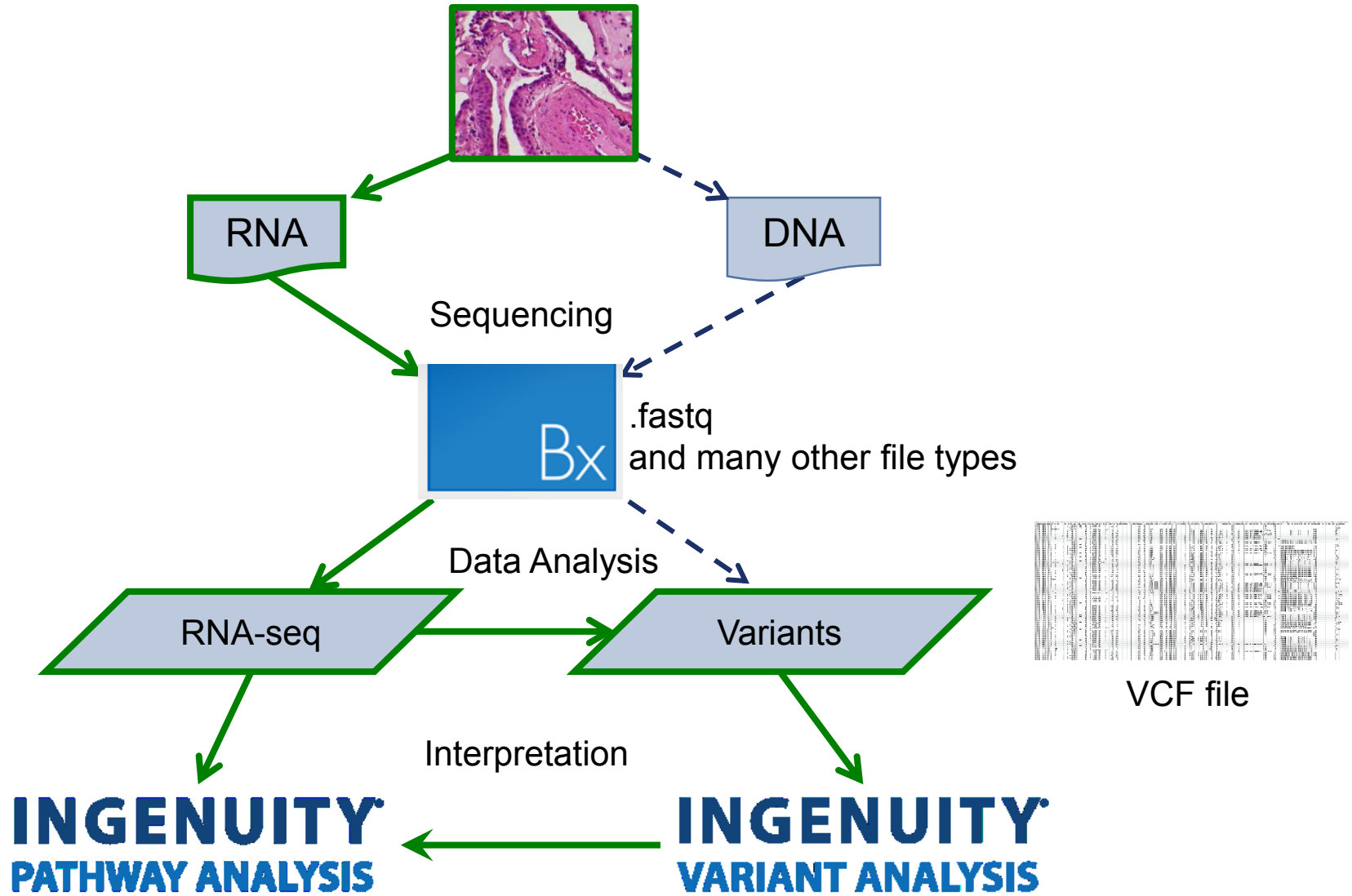
INGENUITY
VARIANT ANALYSIS



Fast and Easy Analysis

















- **Accurate and trustworthy results**
 - ✓ Whole Genome Sequencing
 - ✓ Whole Exome Sequencing
 - ✓ Targeted or Whole Transcriptome Sequencing
 - ✓ ChIP-Seq data
- **Intuitive and easy-in-use**
 - ✓ Comprehensive end-to-end analysis workflows for single samples or cohort studies
 - ✓ One-click analysis of QIAGEN GeneRead DNaseq Amplicon Panels
 - ✓ Streamlined integration with Ingenuity Pathway Analysis (IPA) & Ingenuity Variant Analysis
- **Flexible & customizable**
 - ✓ Ready-to-use workflows can be customized
 - ✓ Build your own workflows



Genomics Workbench

- Analysis of NGS data on ALL organisms
- Reference data management for model organisms: *C. elegans*, *S. cerevisiae*, etc.
- Supports microbial and non-mammalian NGS analysis
- Supports de novo assembly

















- ▶  Genome Finishing Module
- ▶  Ingenuity Pathway Analysis
- ▶  Classical Sequence Analysis
- ▶  Molecular Biology Tools
- ▶  BLAST
- ▶  NGS Core Tools
- ▶  Track Tools
- ▶  Resequencing Analysis
- ▶  Transcriptomics Analysis
- ▶  Epigenomics Analysis
- ▶  De Novo Sequencing
- ▶  Workflows
- ▶  Consulting Track Tools
- ▶  Legacy Tools



Biomedical Workbench

- Tools most relevant to clinical applications on human data
- Automation and Reference Management geared towards for Human research
 - Human, Mouse, Rat
- Ready-to-use work flows

Tools

- ▶  Genome Browser
- ▶  Quality Control
- ▶  Preparing Raw Data
- ▶  Resequencing Analysis
- ▶  Add Information to Variants
- ▶  Remove Variants
- ▶  Add Information to Genes
- ▶  Compare Samples
- ▶  Ingenuity Pathway Analysis
- ▶  Identify Candidate Variants
- ▶  Identify Candidate Genes
- ▶  Expression Analysis
- ▶  Helper Tools
- ▶  Ingenuity Variant Analysis
- ▶  Cloning and Restriction Sites
- ▶  Sanger Sequencing



Streamlined workflows and a rich toolbox to efficiently process data

Toolbox

Ready-to-Use Workflows

- Preparing Raw Data
- Whole Genome Sequencing
- Whole Exome Sequencing
- Targeted Amplicon Sequencing
 - Annotate Variants (TAS)
 - Filter Somatic Variants (TAS)
 - Identify Known Variants in One Sample (TAS)
 - Identify Somatic Variants from Tumor Normal Pair (TAS)
 - Identify Variants (TAS)
 - Identify and Annotate Variants (TAS)
- Whole Transcriptome Sequencing

Tools

- Genome Browser
- Quality Control
- Preparing Raw Data
- Resequencing Analysis
- Add Information to Variants
- Remove Variants
- Add Information to Genes
- Compare Samples
- Ingenuity Pathway Analysis
- Identify Candidate Variants
- Identify Candidate Genes
- Transcriptomics Analysis
- Helper Tools
- Ingenuity Variant Analysis
- Cloning and Restriction Sites
- Sanger Sequencing
- Epigenomics Analysis
- Workflows

Customize workflows

Workflow Input ↓

QC reports

QC for Target Sequencing (Tue Nov 18 19:19:09 GMT 2014)

Version: CLC Cancer Research Workbench 1.5.2

User: tbonnert

Parameters:

- Track of Target Regions = NGH5-003X_Human_Myeloid_Leukemia
- Report type = 1x, 5x, 10x, 20x, 40x, 80x, 100x
- Minimum coverage = 30
- Ignore non-specific matches = Yes
- Ignore broken pairs = Yes
- Create report = Yes
- Create track = Yes
- Create coverage table = No

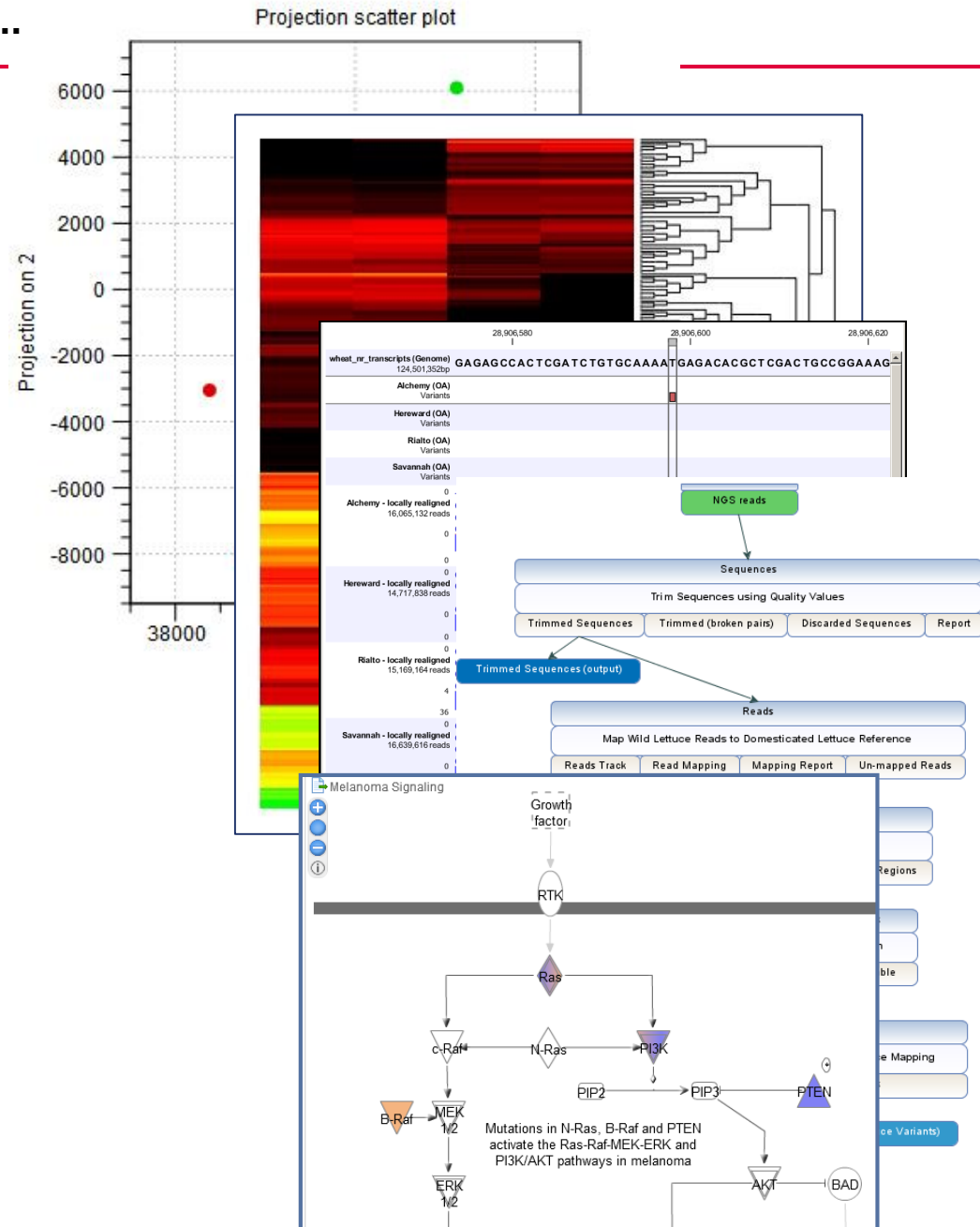
History

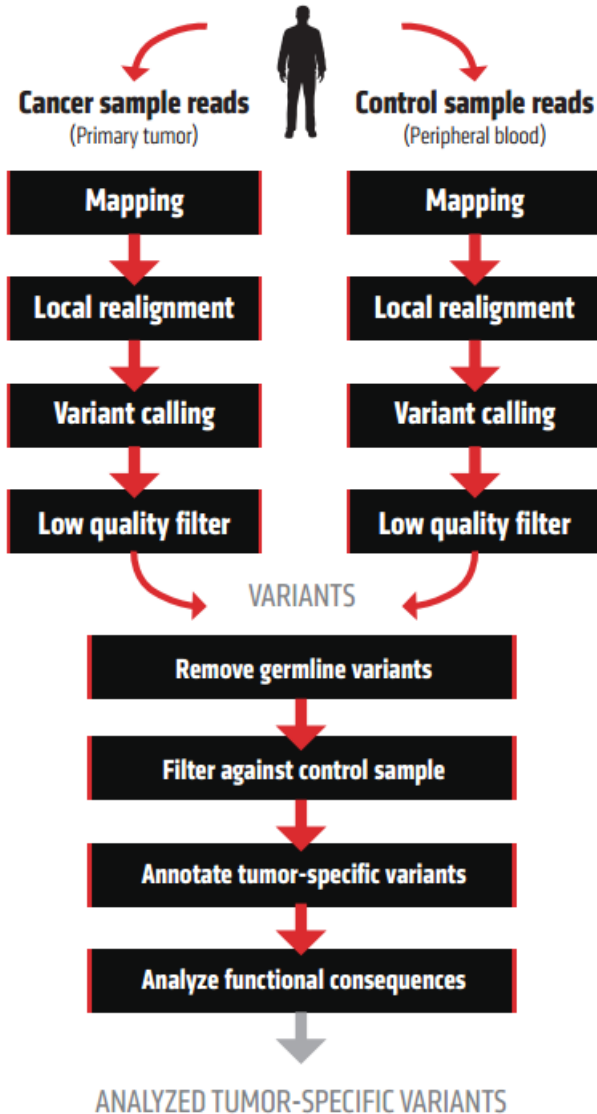
Visualization and Validation

Chromoso...	Region	Type	Reference	Allele	Frequency	Coding region change	Amino acid change	dbSNP
13	32929387	SNV	T	C	99.95	ENST00000544455:c.7397T>C	ENSP00000439902:p.Val2466Ala	169547
17	41246481	SNV	T	C	71.88	ENST00000471181:c.1067A>G	ENSP00000418960:p.Gln356Arg	1722246
17	41258504	SNV	A	C	69.06	ENST00000471181:c.181T>G	ENSP00000418960:p.Cys61Gly	28897672

In CLC Workbenches you can..

1. QC and preprocess NGS data (RNA-Seq, smRNA, and DNaseq reads)
1. Differential expression and statistical analysis for RNA-Seq and smRNA
2. Generate, annotate, and compare high-confidence variant calls
1. Facilitate analysis with interactive visualization
2. Construct automated workflows in user friendly interface
1. Modules [plugins] available for additional or custom functionality





- Matched Tumor/Normal
- Tumor alone
- Tumor vs controls

Ingenuity Variant Analysis integration: two ways!



**Biomedical Genomics
Workbench & Server**



**INGENUITY
VARIANT ANALYSIS**

- Ready to use workflows + Ingenuity Variants Analysis plugin
- Make it one click by leveraging workflow customization!
- Click on the link to see results in IVA
- Edit filtering cascade in IVA and send the result back in BxWB
- Use tracks to compare results from different filter cascades in BxWB

The screenshot displays the Ingenuity Variant Analysis (IVA) interface. At the top, a 'Genome Browse...' window shows genomic coordinates from 66,533,740 to 66,533,800. Below this, several tracks are visible: 'Homo_sapiens_sequen', 'Homo_sapiens_ensem bl_v74_Genes', 'Homo_sapiens_ensem bl_v74_mRNA', and 'Homo_sapiens_ensem bl_v74_CDS'. Two paired-end sequencing reads are shown: SRR719299_1 (paired) trimmed (paired) and SRR719300_1 (paired) trimmed (paired) Read. The SRR719299_1 read is mapped to the tumor sample, and the SRR719300_1 read is mapped to the normal sample. The 'Annotated Somatic Variants' track shows a list of variants with red arrows pointing to the 'Annotated Somatic Variants (IVA)' and 'Annotated Somatic Variants (IVA) (IVA update)' sub-tracks. Below the tracks, a table titled 'Annotated Som...' shows the results of the variant analysis.

Chromosome	Region	Reference	Allele	ESP_AF	ESP_AF_AA	ESP_AF_EA	ASSESSMENT	HGVS_PROT
17	66533811..66533813	CGC	CGC	0.00	0.00	0.00	Likely Pathogenic	p.M339_R34
18	14764045..14764047	TTG	TTG	0.00	0.00	0.00	Uncertain Significance	p.A395T
6	32552086..32552087	TC	AT	0.00	0.00	0.00	Uncertain Significance	p.D57I

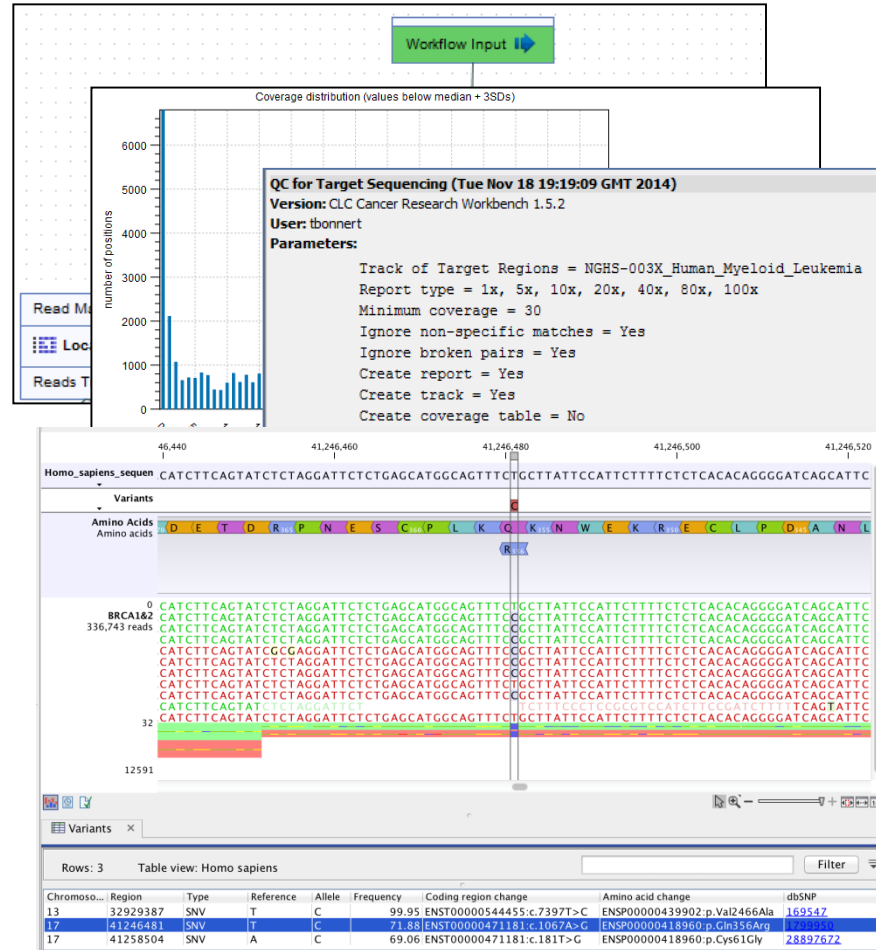
Streamlined workflows and a rich toolbox to efficiently process data

Ready-to-Use Workflows

- Preparing Raw Data
- Whole Genome Sequencing
- Whole Exome Sequencing
 - General Workflows (WES)
 - Somatic Cancer (WES)
 - Hereditary Disease (WES)
 - Filter Causal Variants (WES-HD)
 - Identify Causal Inherited Variants in Family of Four (WES)
 - Identify Causal Inherited Variants in Trio (WES)
 - Identify Rare Disease Causing Mutations in Family of Four (WES)
 - Identify Rare Disease Causing Mutations in Trio (WES)
 - Identify Variants (WES-HD)
 - Identify and Annotate Variants (WES-HD)
 - Identify and Interpret Causal Variants in Family of Four using IVA (WES)
 - Identify and Interpret Causal Variants in Trio using IVA (WES)
- Targeted Amplicon Sequencing
- Whole Transcriptome Sequencing

Tools

- Genome Browser
- Quality Control
- Preparing Raw Data
- Resequencing Analysis
 - Add Information to Variants
 - Remove Variants
 - Add Information to Genes
- Compare Samples
- Identify Candidate Variants
- Identify Candidate Genes
- Expression Analysis
- Helper Tools
- Ingenuity Variant Analysis
- Cloning and Restriction Sites
- Sanger Sequencing
- Epigenomics Analysis



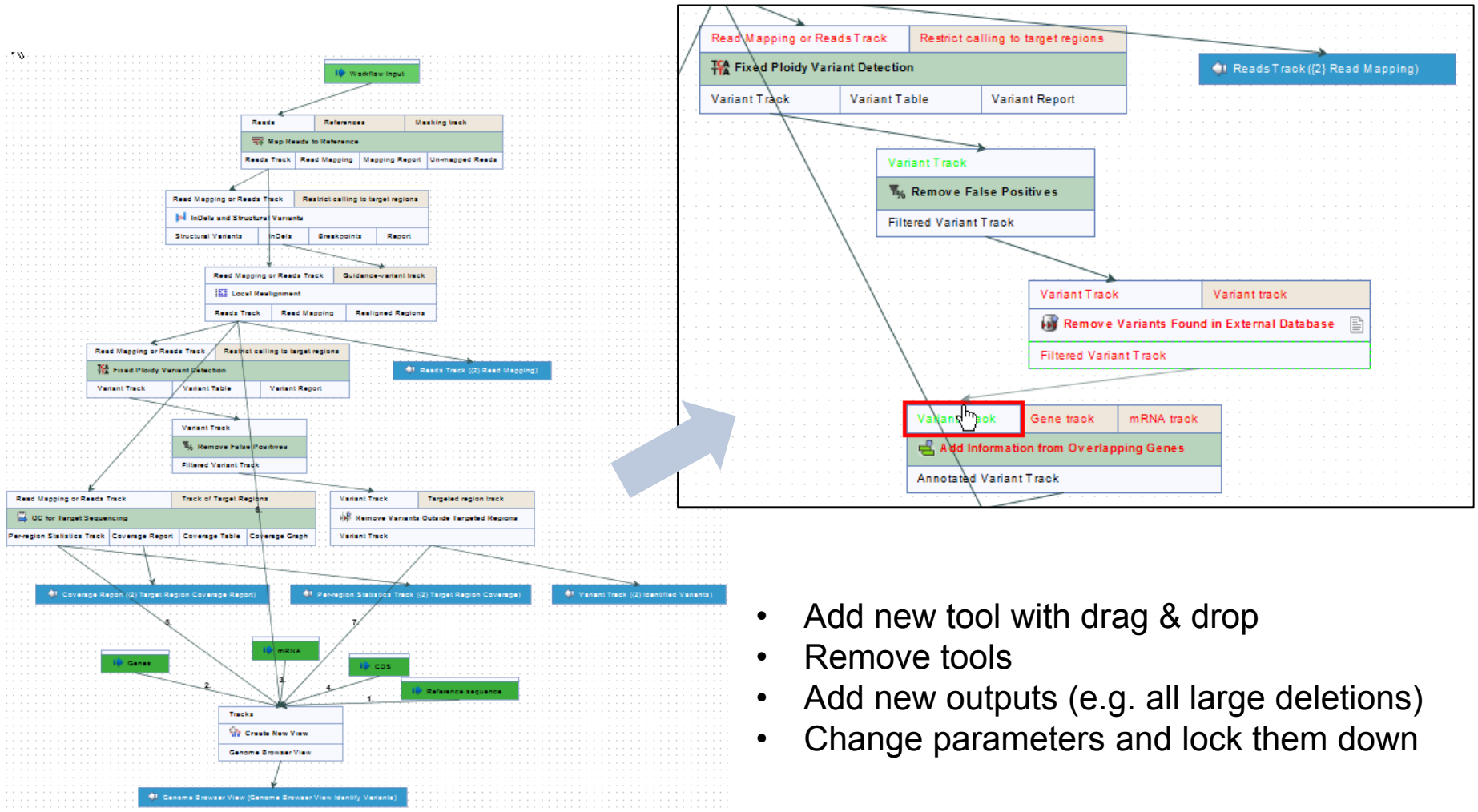
Customize workflows

QC reports

History

Visualization and Validation

Very easy customization of ready-to-use workflows



- Add new tool with drag & drop
- Remove tools
- Add new outputs (e.g. all large deletions)
- Change parameters and lock them down

Lock key parameters of workflow to standardise processing

The image shows a workflow diagram on the left and a configuration dialog box on the right. The workflow starts with 'Workflow Input' leading to 'Reads' (1+), which includes 'Map Reads to Reference'. This leads to 'Read Mapping or Reads Track' (Local Realignment), which then leads to 'Read Mapping or Reads Track' (Low Frequency Variant Detection). This step leads to 'Variant Track' (Remove False Positives), which leads to 'Variant Track' (Filtered Variant Track). Further steps include 'Variant Track' (Remove Variants Out) and 'Variant Track'.

The 'Configure Low Frequency Variant Detection' dialog box is open, showing the following settings:

- 1. Low frequency variant parameters (Low Frequency Variant Detection):**
 - Maximum coverage: 100000
 - Minimum coverage: 10
- 2. General filters (Low Frequency Variant Detection):**
 - Minimum count: 2
 - Minimum frequency (%): 5.0
- Reference masking:**
 - Target regions: [Empty field]
- Read filters:**
 - Ignore broken pairs:
 - Ignore non-specific matches: Reads
 - Minimum read length: 20

Red arrows point to the 'Lock' icons for 'Maximum coverage', 'Minimum coverage', 'Minimum count', and 'Minimum frequency (%)'. Green arrows point to the 'Unlock' icons for 'Minimum coverage' and 'Minimum frequency (%)'. The dialog box has buttons for '?', a refresh icon, 'Previous', 'Next', 'Finish', and 'Cancel'.

Powerful, task-driven, user-friendly tools

Toolbox

Ready-to-Use Workflows

- + Preparing Raw Data
- + Whole Genome Sequencing
- + Whole Exome Sequencing
- + Targeted Amplicon Sequencing
- + Whole Transcriptome Sequencing

Tools

- + Genome Browser
- + Quality Control
- + Preparing Raw Data
- + Resequencing Analysis
- + **Add Information to Variants**
- + **Remove Variants**
- + Add Information to Genes
- + Compare Samples
- + Identify Candidate Variants
- + Identify Candidate Genes
- + Expression Analysis
- + Helper Tools
- + Ingenuity Variant Analysis
- + Cloning and Restriction Sites
- + Sanger Sequencing
- + Epigenomics Analysis
- + Workflows
- + Legacy Tools

- + Add Information from Variant Databases
- + Add Conservation Scores
- + Add Exon Number
- + Add Flanking Sequence
- + Add Fold Changes
- + Add Information about Amino Acid Changes
- + Add Information from Genomic Regions
- + Add Information from Overlapping Genes
- + Link Variants to 3D Protein Structure
- + Download 3D Protein Structure Database
- From Databases
 - + Add Information from 1000 Genomes Project
 - + Add Information from Allele Frequency Community
 - + Add Information from COSMIC
 - + Add Information from ClinVar
 - + Add Information from Common dbSNP
 - + Add Information from HapMap
 - + Add Information from dbSNP

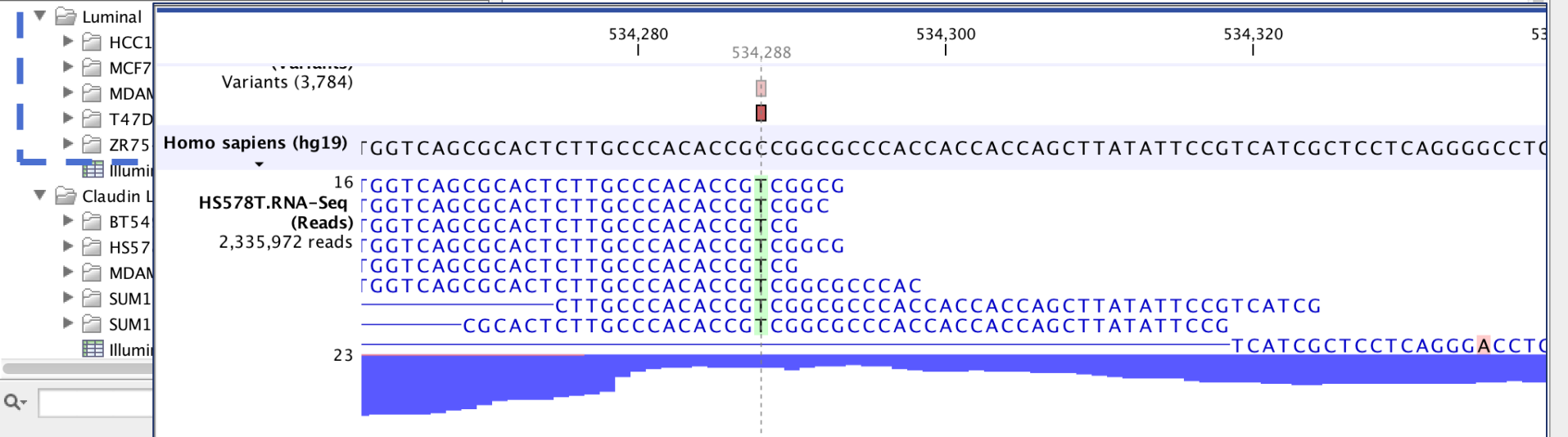
- + Remove Variants Found in External Database
- + Remove Variants Not Found in External Database
- + Remove False Positives
- + Remove Germline Variants
- + Remove Reference Variants
- + Remove Variants Inside Genome Regions
- + Remove Variants Outside Genome Regions
- + Remove Variants Outside Targeted Regions
- From Databases
 - + Remove Variants Found in 1000 Genomes Project
 - + Remove Variants Found in Allele Frequency Community
 - + Remove Variants Found in Common dbSNP
 - + Remove Variants Found in HapMap

Show New Save Import Export Graphics Print Undo Redo Cut Copy Paste Delete

Workspace Plugins Data Management Workflows

Navigation Area

* Copy of Ident... x



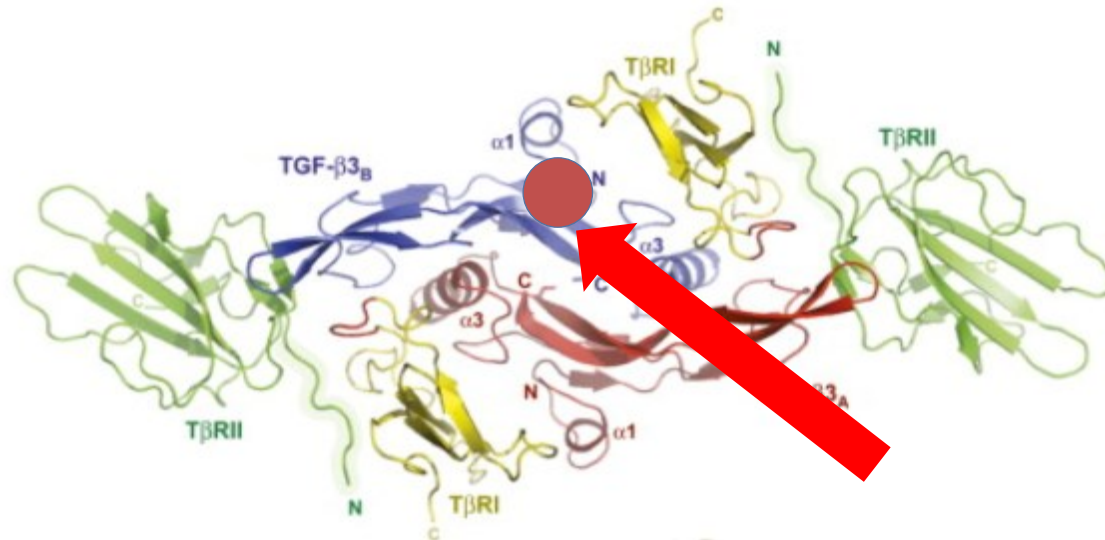
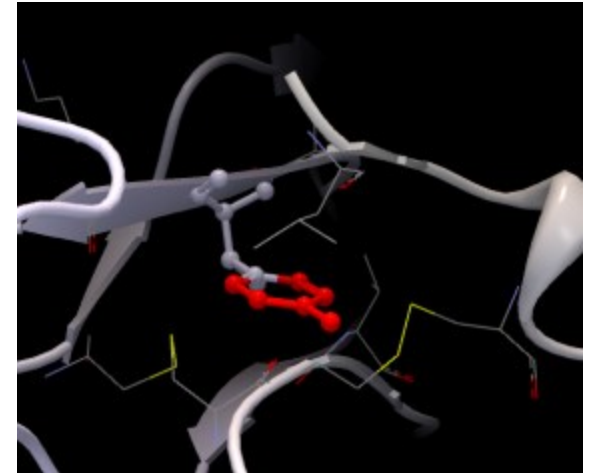
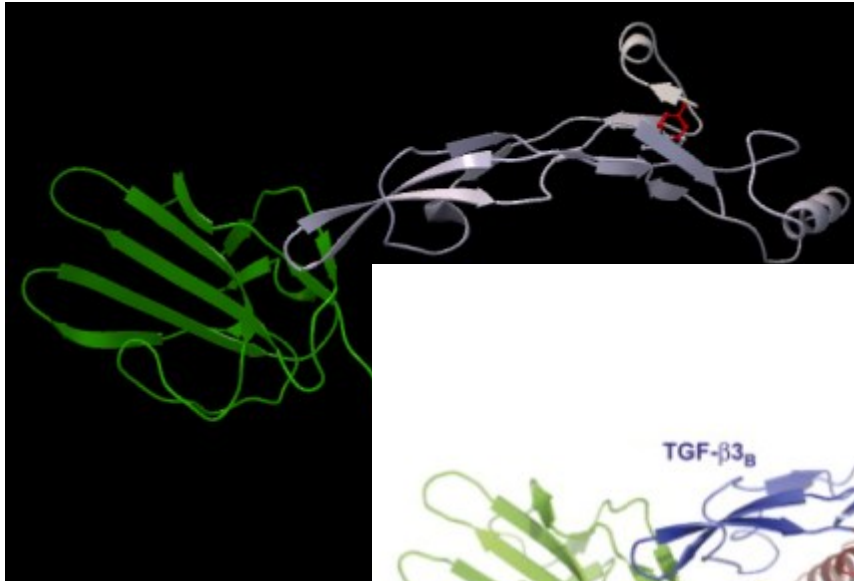
- ▼ Add Information to Variants
 - ▼ Add Information from Variant Databases
 - ▼ Add Conservation Scores
 - ▼ Add Exon Number
 - ▼ Add Flanking Sequence
 - ▼ Add Fold Changes
 - ▼ Add Information about Amino Acid Changes
 - ▼ Add Information from Genomic Regions
 - ▼ Add Information from Overlapping Genes
 - ▼ Link Variants to 3D Protein Structure**

HRAS

Name	ENSEMBL
HRASLS	ENSG00000127252
HRAS	ENSG00000174775
HRASLS5	ENSG00000168004
HRASLS2	ENSG00000133328

0 element(s) are selected

Mutation (in red) disrupt TGF- β 3/TbR1 binding



The screenshot displays the Biomedical Workbench interface. The top menu bar includes options like Show, New, Save, Import, Export, Graphics, Print, Undo, Redo, Cut, Copy, Paste, and Delete. The left sidebar shows a project tree with folders like Luminal, HCC1, MCF7, MDAM, T47D, ZR75, Claudin L, BT54, HS57, MDAM, SUM1, and SUM1. The main workspace shows a genomic track for 'Homo sapiens (hg19)' with a 'Variants (3,784)' track and an 'HS578T.RNA-Seq (Reads)' track. The reads track shows 2,335,972 reads. A 'Select export format' dialog is open in the foreground, listing various export options.

Name	Description	Extension	Supported format
Sequence CSV	Export sequences or sequence lists as Comma...	[csv]	Yes
Tab delimited text	Export tables or tabular information as Tab De...	[txt]	Yes
Table CSV	Export tables in CSV format	[csv]	Yes
VCF	Export variant tracks to Variant Call Format	[vcf]	Yes
Wiggle	Export graph track in Wiggle format	[wig]	Yes
Zip	Export files and folder structure in CLC format ...	[zip]	Yes



Genomic browser view showing variants (3,784) and a sequence alignment for *Homo sapiens (hg19)*. The sequence is: `CGCCACCACCACCAGCTTATATTCCGTCATCGCTCCTCAGGGGCTC`. A blue arrow points from the **Ingenuity Variant Analysis** tool in the **Toolbox** to the sequence alignment.

Toolbox

- Whole Trans
- Annotate
- Compare
- Identify C
- Identify V
- Identify a

Tools

- Genome Bro
- Quality Contr
- Preparing P

Processes

- Idle...

My Samples | My Analyses | Publications

Upload Refresh Share Activate Analyze Annotate Cancer_type = ClaudinLow

Showing 5 samples Cancer_type = ClaudinLow Clear tag

Barcode	Display Name	Description
SUM159PT.s	SUM159PT.sortedByNa...	SUM159PT.sortedByName_1 (paired) RNA-Seq (Reads) - locally realigned (Variants)
SUM1315PT.	SUM1315PT.sortedByNa...	SUM1315PT.sortedByName_1 (paired) RNA-Seq (Reads) - locally realigned (Variants)
MDAMB231.s	MDAMB231.sortedByNa...	MDAMB231.sortedByName_1 (paired) RNA-Seq (Reads) - locally realigned (Variants)
HS578T.sorte	HS578T.sortedByNa...	HS578T.sortedByName_1 (paired) RNA-Seq (Reads) - locally realigned (Variants)
BT549.sorted	BT549.sortedByNa...	BT549.sortedByName_1 (paired) RNA-Seq (Reads) - locally realigned (Variants)

1. QC and preprocess NGS data (RNA-Seq, smRNA, and genomic reads)
2. Differential expression and statistical analysis for RNA-Seq and smRNA
3. Generate, annotate, and compare high-confidence variant calls
4. Facilitate analysis with interactive visualization
5. Construct automated workflows in user friendly interface
6. Modules available for additional or custom functionality
7. Push processed data to Ingenuity and identify pathways affected by genetic variants/expression changes.

QUESTIONS?



4078100 | 20194

× Confidence 4077848 | 20194

× Common Variants 343053 | 14902

× Predicted 850

× Genetic An 208

× Biological 25

Add Filter

- Biological Context
- Cancer Driver Variants
- Common Variants
- Confidence
- Custom Annotation
- Genetic Analysis
- Pharmacogenetics
- Physical Location
- Predicted Deleterious
- Statistical Association
- User-Defined Variants

Chr...	Position	Gene Region	Gene Symbol	Variant	Impact	Consequence	Other
1	39879851	Exonic, Intron	KIAA0754, MA4	p.V1305_A1306	in-frame		
1	39879859	Exonic, Intron	KIAA0754, MA4	p.I1308S	missense		
1	39879877	Exonic, Intron	KIAA0754, MA4	p.P1314S	missense		
1	110121978	Exonic	GN4J3	p.152_153insS*	in-frame		
1	114226255	3'UTR, Exonic	MAGI3	p.I1358fs	frameshift		
1	114226255	3'UTR, Exonic	MAGI3	p.E10236fs, p.E	frameshift		11 116158152
2	179539770	Exonic, Intron	TTN	p.R2074W, p.R2	missense		
2	179640233	Exonic	TTN	p.L421P, p.L446	missense	Damaging	microRNA Bindin MIR216A
3	12475472	Exonic	PPARG				
3	25639332	3'UTR	RARB		stop gain	Tolerated	29 1801166
3	90756702	Exonic	SNCA	p.Y39*	missense	Damaging	
4	112175240	Exonic	APC	p.E1299Q, p.E1	missense	Damaging	microRNA Bindin MIR300, MIR381
5	94486725	Exonic	ROR2	p.E684G			microRNA Bindin MIR381
9	126677081	3'UTR	CTBP2		frameshift	Damaging	1 3
10	32409472	3'UTR	WT1	p.P199fs, p.P48	in-frame	Damaging	
11	64540917	Exonic	SF1	p.P265S	missense	Damaging	
11	125397524	Exonic	UBC	p.S115C	frameshift	Damaging	
12	48902927	Exonic	FBN1	p.P47fs	missense	Damaging	
15	66995733	Exonic, ncRNA	SMAD6	p.D1124N, p.D1	stop gain		
15	17716010	Exonic	SREBF1	p.E12*			
17	17740098	Exonic	SREBF1				

HIPAA
Health Insurance Portability
and Accountability Act

U.S. - EU
SAFE HARBOR

TRUSTe
CERTIFIED PRIVACY

Ingenuity[®] Variant Analysis[™] Overview

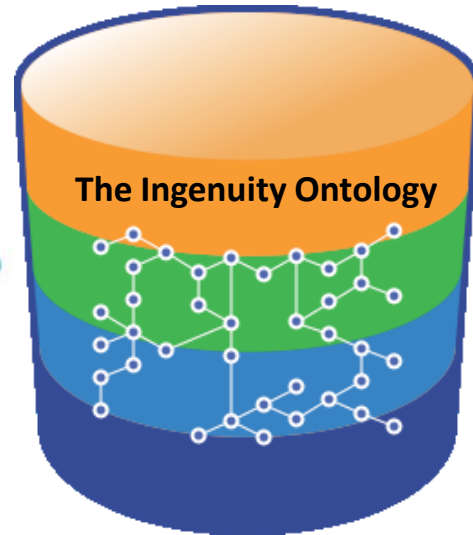
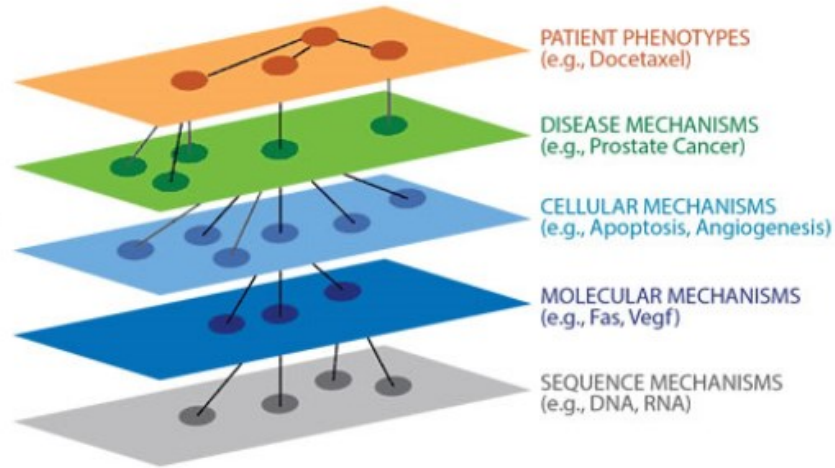
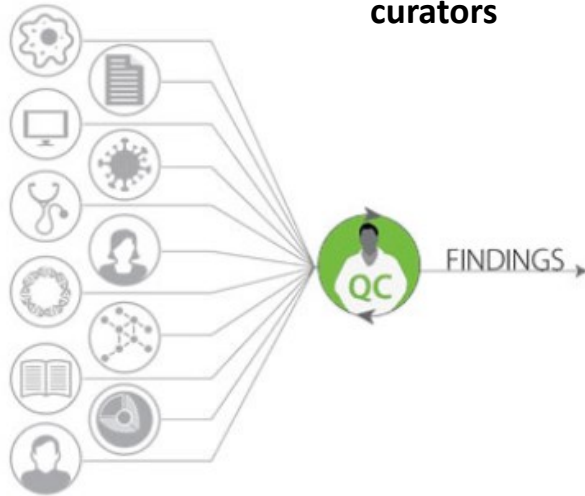
Unprecedented Access to Literature Knowledge

Literature findings

MD/PhD level
curators

Biomedical Ontology

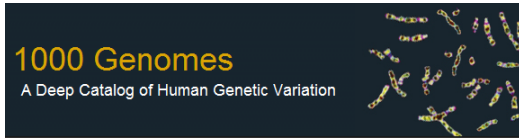
The Ingenuity
Knowledge Base



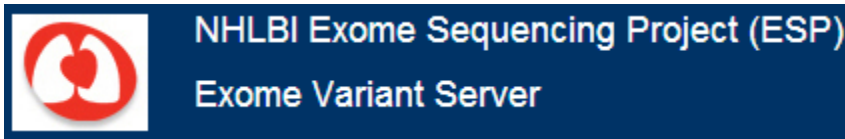
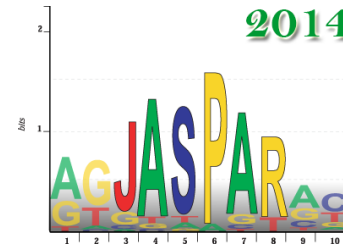
Content Acquisition

Ingenuity Ontology

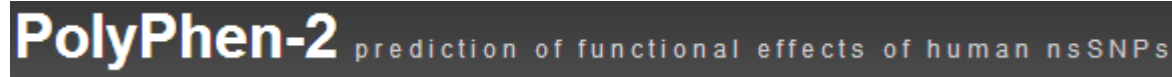
Quality, Context, Coverage, and Timeliness of Content (ca. 1/2014)



Mouse Genome Database

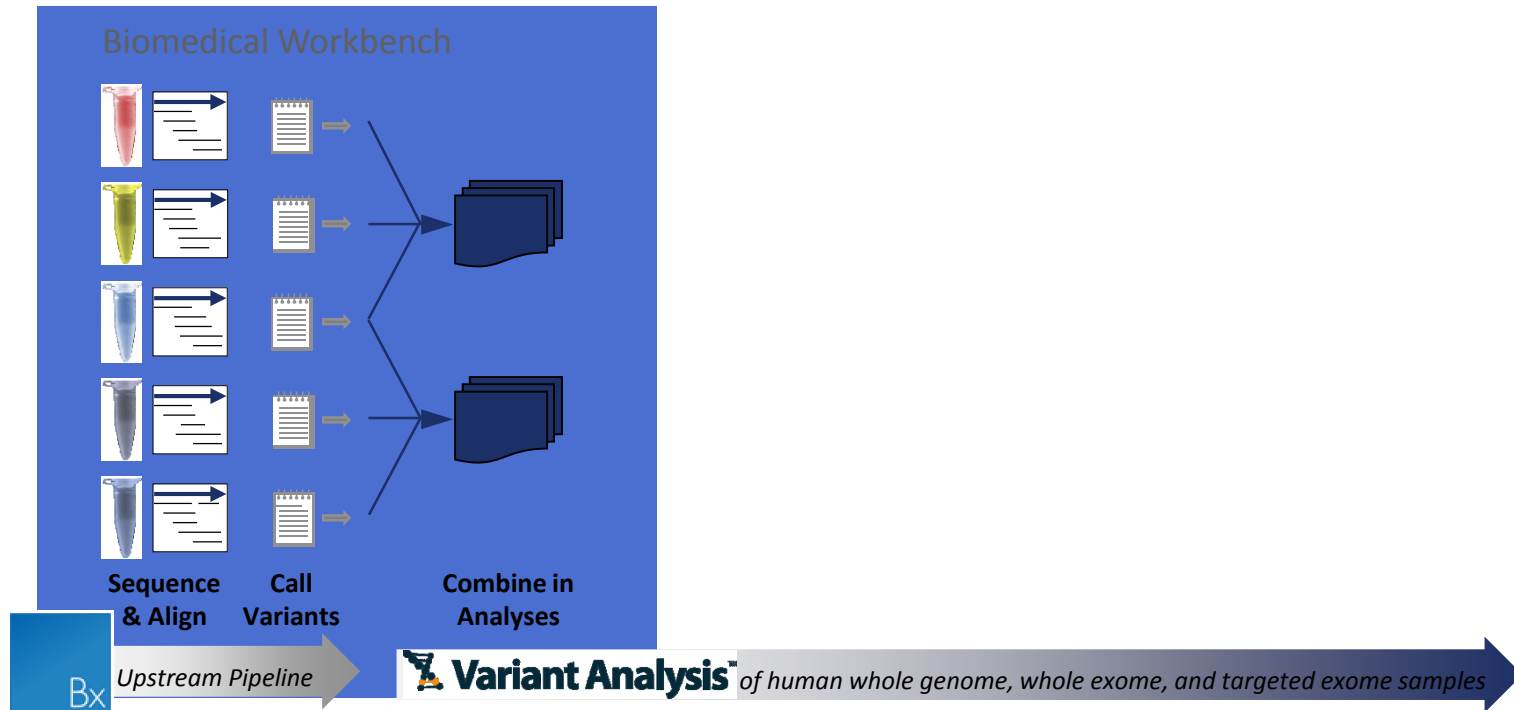


Sorting Intolerant From Tolerant

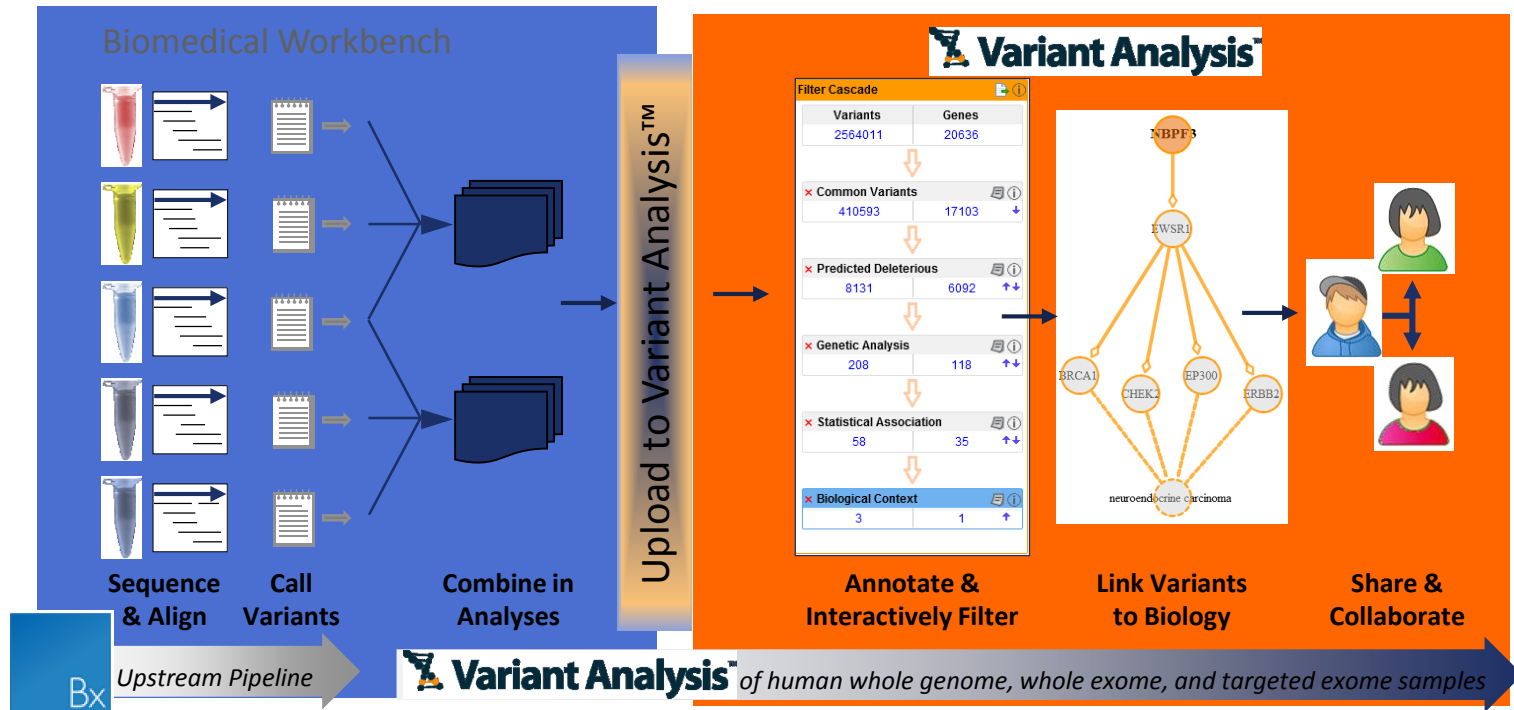


Additionally

- 349,748+ Ph.D./M.D. expert-curated human phenotype-associated mutation findings
- ~3M+ manual literature findings
- 21,458+ curated disease models
- 185,310+ curated pharmacogenetic (PGx) findings



- Identify 'short' list of most plausible variants
 - Causal
 - Biomarkers
- Construct mechanistic hypothesis based on supported biological relationships
- Share with colleagues/ potential collaborators



- Identify ‘short’ list of most plausible variants
 - Causal
 - Biomarkers
- Construct mechanistic hypothesis based on supported biological relationships
- Share with colleagues/ potential collaborators

Filter Cascade

Variants	Genes
46076	9648
↓	
× Confidence	
46076	9648
↓	
× Common Variants	
16809	5996
↓	
× Predicted Deleterious	
5583	3474
↓	
× Genetic Analysis	
38	5
↓	
× Biological Context	
38	5
<input type="checkbox"/> Recalculate when filters change	

Add Filter

Chr...	Position	Gene Region	Gene Symbol	Protein Variant	Case Samples	Control Samples	Translation Impact	SIFT Fu
6	31236668	3'UTR	HLA-C		-----■	-----		
6	31236767	3'UTR	HLA-C		-----■	-----		
6	31236800	3'UTR	HLA-C		-----■	-----		
6	31236821	3'UTR	HLA-C		-----■	-----		
6	31236853	3'UTR	HLA-C		-----■	-----		
6	31236862	3'UTR	HLA-C		-----■	-----		
6	31237773	Exonic	HLA-C	p.T329A	--■---	-----	in-frame	Activat
6	31238027	Exonic	HLA-C	p.M285I	--■---	-----	missense	Dama
6	31238909	Exonic	HLA-C	p.T187L	■-----	-----	in-frame	
6	31238931	Exonic	HLA-C	p.L180L	■-----	-----	synonymous	
6	31238995	Exonic	HLA-C	p.T158T	■-----	-----	synonymous	
6	31239050	Exonic	HLA-C	p.S140Y	---■---	-----	missense	Activat
6	31239100	Exonic	HLA-C	p.S123Y, p.Y123	---■---	-----	in-frame, synonymic	Activat
6	31239101	Exonic	HLA-C	p.S123F, p.Y123	---■---	-----	missense	Tolera
6	31239501	Exonic	HLA-C	p.A73E	---■---	-----	missense	Dama
8	11700213	3'UTR	CTSB		---■---	-----		
8	11700373	3'UTR	CTSB		---■---	-----		
8	11700676	3'UTR	CTSB		---■---	-----		

My Samples | My Analyses | Publications

Filter Cascade

Variants	Genes
46076	9648
↓	
× Confidence	
46076	9648
↓	
× Common Variants	
16809	5996
↓	
× Predicted Deleterious	
5583	3474
↓	
× Genetic Analysis	
38	5
↓	
× Biological Context	
38	5

Recalculate when filters change

Add Filter

Filter x

Confidence **Rename**

Keep only variants which satisfy all of these criteria:

- Call quality is at least in any case or at least in any control
- AND
- Variant passed upstream pipeline filtering
- AND
- Read depth is at least in any sample
- AND
- Allele fraction is at least % in any sample
- AND
- Outside top % most exonically variable 100base windows in healthy public genomes
- AND
- Outside top % **most exonically variable genes** in healthy public genomes (1000 Genomes)

Subsequent filters only treat a variant as present for samples that also satisfy the Keep criteria.

Apply

Legend [\[show\]](#)

My Samples | My Analyses | Publications

Filter Cascade
📄 ⓘ

Variants	Genes
46076	9648
↓	
× Confidence ⓘ	
46076	9648 ↓
↓	
× Common Variants ⓘ	
16809	5996 ↑↓
↓	
× Predicted Deleterious ⓘ	
5583	3474 ↑↓
↓	
× Genetic Analysis ⓘ	
38	5 ↑↓
↓	
× Biological Context ⓘ	
38	5 ↑

Recalculate when filters change

Add Filter

Legend [\[show\]](#)

Filter
✕

Rename

Exclude variants that are observed in any of these populations with an allele frequency of

- at least 3 % in the 1000 Genomes Project
- at least 3 % in the ExAC
- at least 3 % of all NHLBI ESP exomes
- at least 3 % in the Allele Frequency Community (includes ExAC and CGI)

OR

are present in dbSNP

* The public Complete Genomics genomes are included in the AFC

Apply

My Samples | My Analyses | Publications

Filter Cascade

Variants	Genes
46076	9648
↓	
× Confidence	
46076	9648
↓	
× Common Variants	
16809	5996
↓	
× Predicted Deleterious	
5583	3474
↓	
× Genetic Analysis	
38	5
↓	
× Biological Context	
38	5

Recalculate when filters change

Add Filter

Predicted Deleterious

Keep only variants that are experimentally observed to be associated with a phenotype:

Disease-associated according to computed ACMG Guidelines classification

- Pathogenic
- Likely Pathogenic
- Uncertain Significance
- Likely Benign
- Benign
- Listed in HGMD®

OR

are associated with gain of function of a gene

- Established in the Literature
- Gene Fusion
- Inferred activating mutation by Ingenuity
- Predicted gain of function by BSIFT
- microRNA Binding Site
- Copy Number Gain

OR

are associated with loss of function of a gene

- Frameshift, in-frame indel, or start/stop codon change
- Missense unless predicted tolerated by SIFT or PolyPhen-2
- Nullizygous
- Splice site loss up to bases into intron or as predicted by MaxEntScan
- Deleterious to a microRNA

Apply

Legend [show]

[My Samples](#) | [My Analyses](#) | [Publications](#)

Filter Cascade
📄 ⓘ

Variants	Genes
46076	9648

↓

× Confidence
📄 ⓘ

46076	9648	↓
-------	------	---

↓

× Common Variants
📄 ⓘ

16809	5996	↑↓
-------	------	----

↓

× Predicted Deleterious
📄 ⓘ

5583	3474	↑↓
------	------	----

↓

× Genetic Analysis
📄 ⓘ

38	5	↑↓
----	---	----

↓

× Biological Context
📄 ⓘ

38	5	↑
----	---	---

↓

Recalculate when filters change

Add Filter

[Legend \[show\]](#)

Filter
✕

Genetic Analysis
Rename

Use recommended settings for: (Custom) Tumor-specific variants Set

Pair/match samples from the same individual

Restrict to transmitted variants

Case Samples

Keep only variants which are

associated with gain of function
To control specific gain of function types, use the Predicted Deleterious filter

OR

Homozygous
 Compound Heterozygous
 Haploinsufficient
 Hemizygous
 Nullizygous

Het-ambiguous
 Heterozygous

AND

the genotypes selected above occur in at least 2 of the 5 case samples (40%) at gene level

Control Samples

Exclude variants which are

associated with gain of function
To control specific gain of function types, use the Predicted Deleterious filter

OR

Homozygous
 Compound Heterozygous
 Haploinsufficient
 Hemizygous

Het-ambiguous
 Heterozygous

AND

the genotypes selected above occur in at least 1 of the 5 control samples (20%) at variant level

Apply

My Samples | My Analyses | Publications

Filter Cascade

Variants	Genes
46076	9648
↓	
× Confidence	
46076	9648
↓	
× Common Variants	
16809	5996
↓	
× Predicted Deleterious	
5583	3474
↓	
× Genetic Analysis	
38	5
↓	
× Biological Context	
38	5

Recalculate when filters change

Add Filter

Legend [show]

Filter

Biological Context **Rename**

Keep only **variants**

within **1 hop** **upstream**

that are known or predicted to

Affect

genes listed below or genes implicated in the following diseases, processes, pathways, phenotypes, domains, activities, or biomarkers

Enter and select term

× epithelial-mesenchymal transition [process]

Genes

- 3,3'-diindolylmethane
- ABL1
- AGT
- AKT1
- AKT2
- AKT3
- ALX1
- AMELX
- ARHGAP21
- beta-estradiol
- BMI1
- BMP2
- BMP7
- bosutinib
- C1orf61
- CAV1
- CD44
- CDC42
- CDH1
- CDH11
- CLIC4

Upload gene list file(s)...

and genes within **1 hop** **downstream** of above

include diseases consistent with the phenotypes above

Apply

Filter Cascade

Variants	Genes
46076	9648
↓	
Confidence	
44561	9564
↓	
Common Variants	
8020	3152
↓	
Predicted Deleterious	
532	505
↓	
Genetic Analysis	
16	11
↓	
Biological Context	
5	2

Recalculate when filters change

Add Filter

Legend [show]

- Biolog
- Cance
- Comm
- Confic
- Custo
- Genet
- Pharm
- Physi
- Predic
- Statis
- User-I

Filter x

Cancer Driver Variants **Rename**

Keep only variants that are found in

- Cancer-associated mouse knockout phenotypes
[View list of phenotypes](#)
- Cancer-associated cellular processes with
- Cancer-associated pathways with
- Cancer therapeutic targets
[View list of drug targets](#)
- Published cancer literature findings
- Known or predicted cancer subnetwork regulatory sites
[View list of disease genes](#)
- COSMIC at a frequency 0.1 %
- TCGA at a frequency 0.1 %

AND

Involved in any of the diseases listed below

- Breast Cancer

Apply

Filter Cascade

Variants	Genes
46076	9648
↓	
Confidence	
44561	9564
↓	
Common Variants	
8020	3152
↓	
Predicted Deleterious	
532	505
↓	
Genetic Analysis	
16	11
↓	
Biological Context	
5	2

Recalculate when filters change

Add Filter

Chr...	Position	Gene Region	Gene Symbol	Protein Variant	Case Samples	Control Sample
11	534288	Exonic	HRAS	p.G12D	-- -- -- --	-- -- -- --
17	7577099	Exonic	TP53	p.R121K, p.R148	-- -- -- --	-- -- -- --
17	7577534	Exonic	TP53	p.R117S, p.R210	-- -- -- --	-- -- -- --
17	7578461	5'UTR, Exonic	TP53	p.V118F, p.V157	-- -- -- --	-- -- -- --
17	7578526	5'UTR, Exonic	TP53	p.C135F, p.C3F	-- -- -- --	-- -- -- --

Legend [hide]

Function		Confident Call
loss	normal	gain
No		Yes
<ul style="list-style-type: none"> — Identical to Reference Genome █ Heterozygous Variant █ Heterozygous/Ambiguous █ Homozygous Variant █ Copy Number Gain/Heterozygous █ Copy Number Gain/Homozygous █ Hemizygous █ Nullizygous █ Gene Fusion █ No genotype 		<ul style="list-style-type: none"> █ █

Variant: chr11 | 534288 | SNV

View : [More Details](#)
[Path to Phenotype](#)
[Variant Findings \(60\)](#)
[Pharmacogenetics \(375\)](#)

Gene Symbol : **HRAS**
 Harvey rat sarcoma viral oncogene homolog

dbSNP ID : [104894230](#)
 Cytoband : p15.5
 COSMIC ID : [484](#) [Validate]
 99915

Position : chr11:534288 [IGV] [UCS]
 HGMD : [CM081305](#)

Classification : [Uncertain Significance](#)

Gene Region : Exonic
 Protein Variant : p.G12D
 Transcript Variant : c.35G>A
 Translation Impact : missense
 SIFT Function Prediction : Damaging
 PolyPhen-2 Function : Benign

Filter Cascade

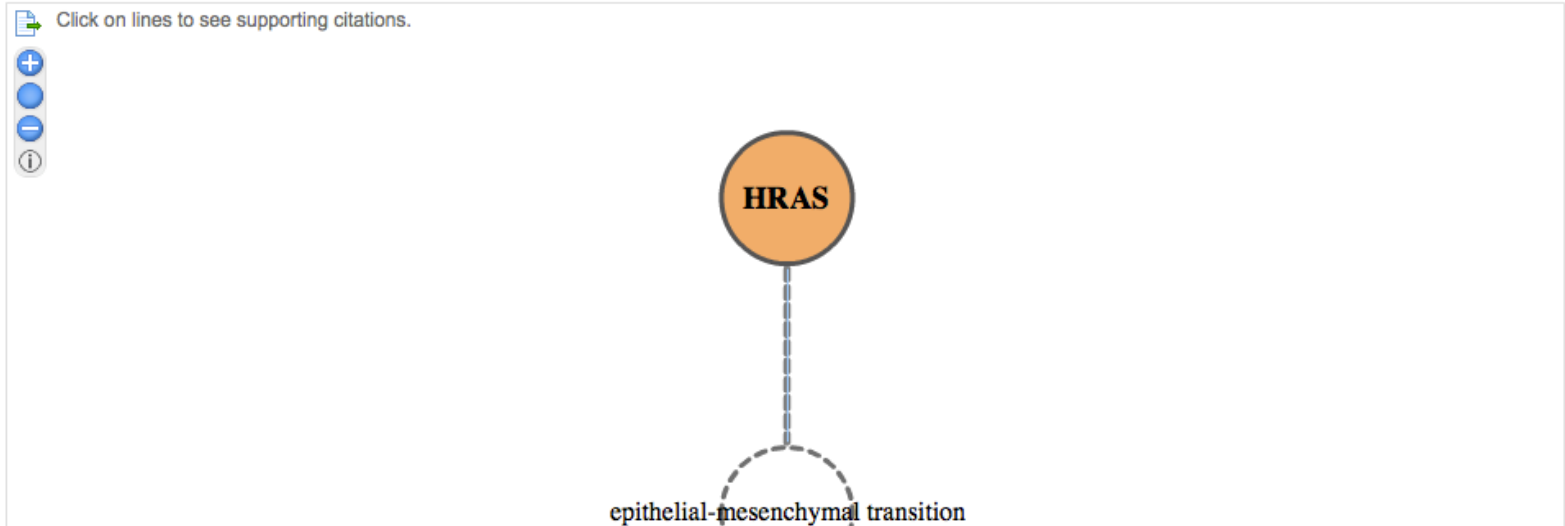
Variants	Genes
46076	9648
↓	
Confidence	
44561	9564

Chr...	Position	Gene Region	Gene Symbol	Protein Variant	Case Samples	Control Sample
11	534288	Exonic	HRAS	p.G12D	-- -- --	-----
17	7577099	Exonic	TP53	p.R121K, p.R148G	-----	-----
17	7577534	Exonic	TP53	p.R117S, p.R216C	-----	-----

Variant: chr11 | 534288 | SNV

View: [More Details](#)
[Path to Phenotype](#)
[Variant Findings \(60\)](#)
[Pharmacogenetics \(375\)](#)

Variant: chr11 | 534288 | p15.5 | SNV | T



symbol: **HRAS**
 Harvey rat sarcoma viral oncogene homolog

NP ID: [104894230](#)
 band: p15.5
 MIC ID: [484](#) [Validate]
 99915
 position: chr11:534288 [IGV] [UCS]
 HGMD: [CM081305](#)

Classification: [Uncertain Significance](#)

Gene Region: Exonic
 Protein Variant: p.G12D
 Mutational Variant: c.35G>A
 Translation Impact: missense
 Function Prediction: Damaging
 PolyPhen-2 Function: Benign

Findings (1 citations)

Expression of activated M-Ras in a murine mammary epithelial cell line induces epithelial-mesenchymal transition and tumorigenesis. *Oncogene*. (2004)

- Activated mutant **HRAS** protein (p.G12V) increases epithelial mesenchymal transition of SCp2 cells.

Filter Cascade

Variants	Genes
46076	9648
↓	
Confidence	
44561	9564

Edit Columns Export Create List Search gene, chr, or dbSNP 5 variants

Chr...	Position	Gene Region	Gene Symbol	Protein Variant	Case Samples	Control Sample
11	534288	Exonic	HRAS	p.G12D	-- -- --	-----
17	7577099	Exonic	TP53	p.R121K, p.R148G	-----	-----
17	7577534	Exonic	TP53	p.R117S, p.R216C	-----	-----

Variant: chr11 | 534288 | SNV

- View: [More Details](#)
- [Path to Phenotype](#)
- [Variant Findings \(60\)](#)
- [Pharmacogenetics \(375\)](#)

Symbol: **HRAS**
Harvey rat sarcoma viral oncogene homolog

dbSNP ID: [104894230](#)
Cytoband: [p15.5](#)
SMIC ID: [484 \[Validate\]](#)
99915
Position: [chr11:534288 \[IGV\]](#) [UCS]
HGMD: [CM081305](#)

Classification: [Uncertain Significance](#)
Gene Region: Exonic
Protein Variant: p.G12D
Nucleotide Variant: c.35G>A
Translation Impact: missense
T Function Prediction: Damaging
PolyPhen-2 Function: Benign

Variant: chr11 | 534288 | p15.5 | SNV | T

Findings (40 citations)

[The Exomes of the NCI-60 Panel: A Genomic Resource for Cancer Biology and Systems Pharmacology. *Cancer Res.* \(2013\)](#)

- Somatic missense heterozygous mutant human **HRAS** gene (c.35G>A translating to p.G12D) is associated with carcinoma in human breast (observed in 1 of 1 samples).
- Somatic missense heterozygous mutant human **HRAS** gene (c.35G>A translating to p.G12D) is associated with carcinoma in human breast (observed in 1 of 1 samples).

[Frequent Mutation of the PI3K Pathway in Head and Neck Cancer Defines Predictive Biomarkers. *Cancer Discov.* \(2013\)](#)

- Somatic missense mutant human **HRAS** gene (c.35G>A translating to p.G12D) is associated with squamous-cell carcinoma in human head and neck (observed in 2 of 7 samples).
- Somatic missense mutant human **HRAS** gene (c.35G>A translating to p.G12D) is associated with squamous-cell carcinoma in human head and neck (observed in 2 of 7 samples).

[RAS Mutations Are Associated With the Development of Cutaneous Squamous Cell Tumors in Patients Treated With RAF Inhibitors. *J Clin Oncol.* \(2012\)](#)

- Somatic missense mutant human **HRAS** gene (c.35G>A translating to p.G12D) is associated with keratoacanthoma in skin from human chest (observed in 1 of 1 samples).

[RAS mutations in cutaneous squamous-cell carcinomas in patients treated with BRAF inhibitors. *N Engl J Med.* \(2012\)](#)

- Somatic missense mutant human **HRAS** gene (c.35G>A translating to p.G12D) is associated with keratoacanthoma in skin from human leg (observed in 1 of 4 samples).
- Somatic missense mutant human **HRAS** gene (c.35G>A translating to p.G12D) is associated with keratoacanthoma in skin from human torso (observed in 1 of 7 samples).

[Postzygotic HRAS and KRAS mutations cause nevus sebaceous and Schimmelpenning syndrome. *Nat Genet.* \(2012\)](#)

- Mutant human **HRAS** gene (c.35G>A) is associated with nevus sebaceous in human.

[HRAS mutants identified in Costello syndrome patients can induce cellular senescence: possible implications for the pathogenesis of Costello syndrome. *J Hum Genet.* \(2011\)](#)

- Change of function heterozygous germline mutant human **HRAS** protein (p.G12D, alternately c.35G>A) is observed with childhood-onset Costello syndrome in human (unknown geographic location).

[Frequent mutations of chromatin remodeling genes in transitional cell carcinoma of the bladder. *Nat Genet.* \(2011\)](#)

- Somatic missense mutant human **HRAS** gene (c.35G>A translating to p.G12D) is associated with carcinoma in human urinary bladder (observed in 2 of 11 samples).
- Somatic missense mutant human **HRAS** gene (c.35G>A translating to p.G12D) is associated with carcinoma in human urinary bladder (observed in 2 of 11 samples).

Filter Cascade

Variants	Genes
46076	9648

↓

Confidence

44561	9564
-------	------

↓

Common Variants

8020	3152
------	------

↓

Predicted Deleterious

532	505
-----	-----

↓

Genetic Analysis

Chr...	Position	Gene Region	Gene Symbol	Protein Variant	Case Samples	Control Sample
11	534288	Exonic	HRAS	p.G12D	-- -- --	-- -- --
17	7577099	Exonic	TP53	p.R121K, p.R148	-- -- --	-- -- --
17	7577534	Exonic	TP53	p.R117S, p.R210	-- -- --	-- -- --
17	7578461	5'UTR, Exonic	TP53	p.V118F, p.V157	-- -- --	-- -- --
17	7578526	5'UTR, Exonic	TP53	p.C135F, p.C3F	-- -- --	-- -- --

Variant: chr11 | 534288 | SNV

View : [More Details](#)
[Path to Phenotype](#)
[Variant Findings \(60\)](#)
[Pharmacogenetics \(375\)](#)

Gene Symbol : **HRAS**
 Harvey rat sarcoma viral oncogene homolog

dbSNP ID : [104894230](#)
 Cytoband : p15.5
 COSMIC ID : [484](#) [Validate]
 99915

Position : chr11:534288 [IGV] [UCS]
HGMD : CM081305

Classification : [Uncertain Significance](#)

HGMD® Professional 2014.1



HGMD accession	Disease/phenotype	Gene symbol	Codon change	Amino acid change	Codon number	Feedback
CM081305	Costello syndrome	HRAS	GGC-GAC	Gly-Asp	12	Feedback

The G12D substitution exhibits a shift in polarity from non-polar to negatively charged and displays a decrease in Kyte-Doolittle hydrophobicity from -0.4 to -3.5. Approximately 1.95% of missense mutations in HGMD are Gly-Asp. The mutation occurs 178 amino acids from the end of the protein.

Literature citation	Citation type	Notes
1. Lo (2008) <i>J Med Genet</i> 45 : 167 PubMed: 18039947	Primary literature report	None
2. Niihori (2011) <i>J Hum Genet</i> 56 : 707 PubMed: 21850009	Functional characterisation	None
3. Cheng (2012) <i>PLoS Comput Biol</i> 8 : e1002738 PubMed: 23093928	Functional characterisation	Systemic impact quantified as a combination of protein stability change and pathway perturbation.

Extra information

Coding strand genomic sequence (GRCh37.3) CGGAATATAAGCTGCTGGTGGTGGCGCCGCGAAGAGTGGCTGACCATCCA

Filter Cascade

Variants	Genes
46076	9648
↓	
Confidence	
44561	9564
↓	
Common Variants	
8020	3152
↓	
Predicted Deleterious	
532	505
↓	
Genetic Analysis	
16	11
↓	
Biological Context	
5	2

Recalculate when filters change

Add Filter

Legend [\[show\]](#)

Summary | Variants | Genes | Groups/Complexes | Pathways | Processes | Diseases | Overview

Share **Publish**

Edit Columns **Export** **Create List** 5 variants

Chr...	Position	Gene Region	Gene Symbol	Protein Variant	Case Samples	Control Sample
11	534288	Exonic	HRAS	p.G12D	- - - - -	- - - - -
17	7577099	Exonic	TP53	p.R121K, p.R148	- - - - -	- - - - -
17	7577534	Exonic	TP53	p.R117S, p.R210	- - - - -	- - - - -
17	7578461	5'UTR, Exonic	TP53	p.V118F, p.V157	- - - - -	- - - - -
17	7578526	5'UTR, Exonic	TP53	p.C135F, p.C3F	- - - - -	- - - - -

Variant: chr11 | 534288 | SNV

View: [More Details](#)
[Path to Phenotype](#)
[Variant Findings \(60\)](#)
[Pharmacogenetics \(375\)](#)

Gene Symbol: **HRAS**
 Harvey rat sarcoma viral oncogene homolog

dbSNP ID: [104894230](#)
 Cytoband: p15.5
 COSMIC ID: [484](#) [\[Validate\]](#)
 99915
 Position: [chr11:534288](#) [\[IGV\]](#) [\[UCS\]](#)
 HGMD: [CM081305](#)

Classification: [Uncertain Significance](#)
 Gene Region: Exonic
 Protein Variant: p.G12D
 Transcript Variant: c.35G>A
 Translation Impact: missense
 SIFT Function Prediction: Damaging
 PolyPhen-2 Function: Benign

Filter Cascade

Variants	Genes
46076	9648

↓

× Predicted Deleterious

532	505
-----	-----

↓

× Genetic Analysis

16	11
----	----

↓

× Biological Context

5	2
---	---

Recalculate when filters change

Chr...	Position	Gene Region	Gene Symbol	Protein Variant	Case Samples	Control Sample
11	534288	Exonic	HRAS	p.G12D	---	---

Name	p-value	#Genes	#Variants	#Cases	%Cases	#Controls	%Controls
Mdm2-Tp53-ubiquitin	1.680E-4	1	4	4	80	0	0
Mdm2-Tp53-Mdm4	2.520E-4	1	4	4	80	0	0
IkB-Tp53	4.200E-4	1	4	4	80	0	0
Ras	5.039E-4	1	1	2	40	0	0
Hd-neuronal intranuclear inclusions	1.260E-3	1	4	4	80	0	0

Variant: chr11 | 534288 | SNV

View: [More Details](#)
[Path to Phenotype](#)
[Variant Findings \(60\)](#)
[Pharmacogenetics \(375\)](#)

Gene Symbol: **HRAS**
 Harvey rat sarcoma viral oncogene homolog

dbSNP ID: [104894230](#)
 Cytoband: p15.5
 COSMIC ID: [484](#) [Validate]
 99915
 Position: chr11:534288 [IGV] [UCS]
 HGMD: [CM081305](#)

Classification: **Uncertain Significance**
 Gene Region: Exonic
 Protein Variant: p.G12D
 transcript Variant: c.35G>A
 Translation Impact: missense
 SIFT Function Prediction: Damaging
 PolyPhen-2 Function: Benign

Filter Cascade

Variants	Genes
46076	9648

↓

Confidence

44561	9564
-------	------

↓

Common Variants

8020

↓

Predicted Deletions

532

↓

Genetic Analysis

16

↓

Biological Context

5

Recalculate when... **Add Filter**

Legend [show]

Chr...	Position	Gene Region	Gene Symbol	Protein Variant	Case Samples	Control Sample
11	534288	Exonic	HRAS	p.G12D	-- -- --	-- -- --
17	7577099	Exonic	TP53	p.R121K, p.R148G	-- -- --	-- -- --

Variant: chr11 | 534288 | SNV

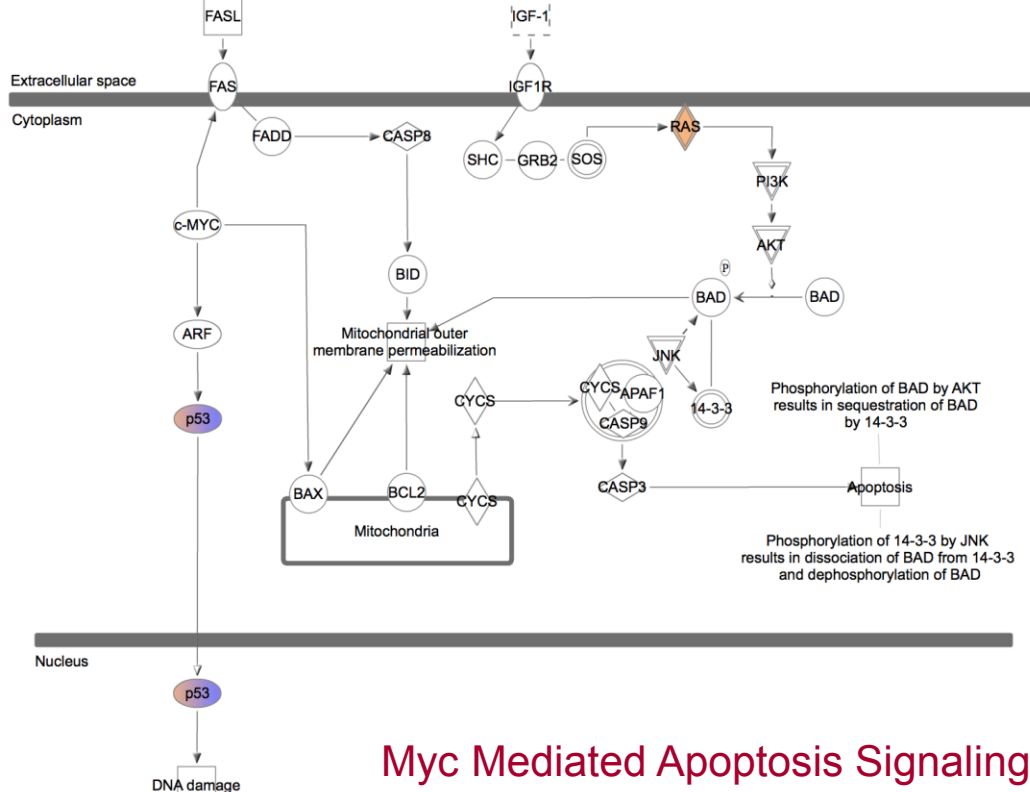
View: [More Details](#) [Path to Phenotype](#) [Variant Findings \(60\)](#) [Pharmacogenetics \(375\)](#)

RAS
Survey rat sarcoma viral oncogene homolog

4894230
5.5
4 [Validate]
915
11:534288 [IGV] [UCS]
1081305

Uncertain Significance

Exonic
p.G12D
c.35G>A
missense
Damaging
Benign



Myc Mediated Apoptosis Signaling

Filter Cascade

Variants	Genes
46076	9648
↓	
Confidence	
44561	9564
↓	
Common Variants	
8020	3152
↓	
Predicted Deleterious	
532	505
↓	
Genetic Analysis	
16	11
↓	
Biological Context	
5	2

Recalculate when filters change

Add Filter

Edit Columns Export Create List Search gene, chr, or dbSNP 5 variants

Chr...	Position	Gene Region	Gene Symbol	Protein Variant	Case Samples	Control Sample
11	534288	Exonic	HRAS	p.G12D	-- -- --	-----
17	7577099	Exonic	TP53	p.R121K, p.R148	-----	-----
17	7577534	Exonic	TP53	p.R117S, p.R210	-----	-----

Variant: chr11 | 534288 | SNV

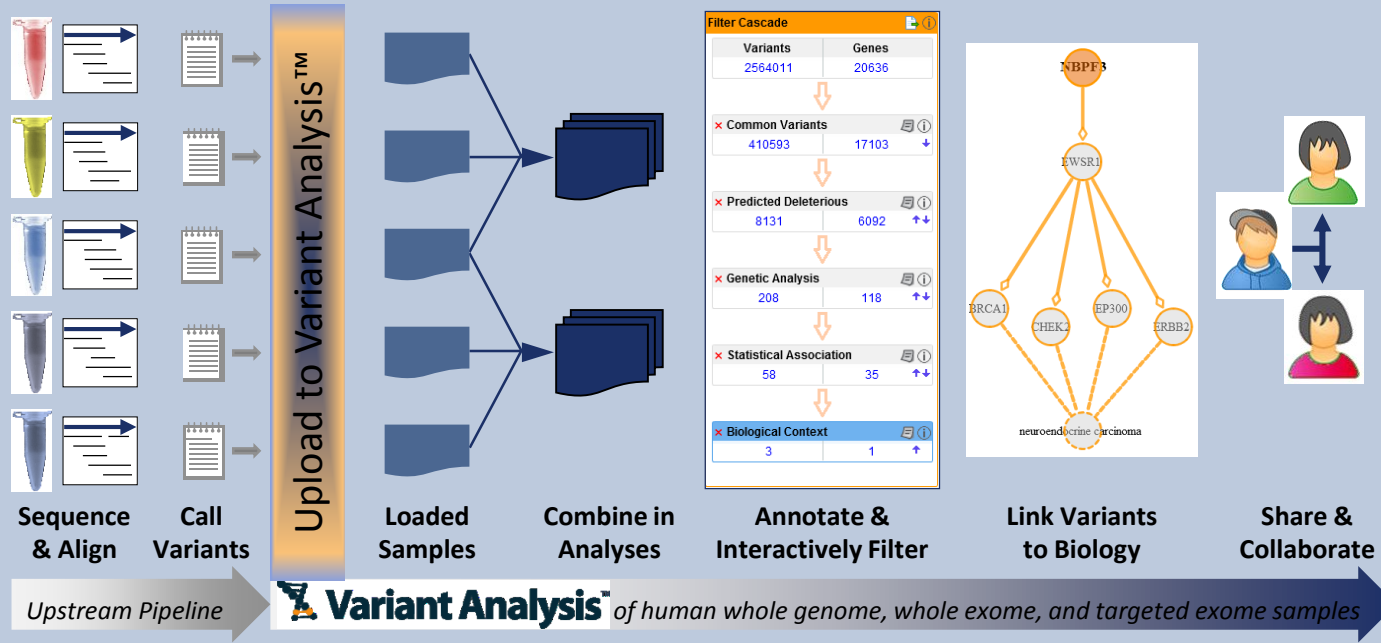
View : [More Details](#)
[Path to Phenotype](#)
[Variant Findings \(60\)](#)
[Pharmacogenetics \(375\)](#)

Name	p-value	#Genes	#Variants	#Cases	%Cases	#Controls	%Controls
arrest in G1/S phase transition of embryonic cell lin	1.058E-8	2	5	5	100	0	0
arrest in developmental process of kidney cell lines	3.528E-8	2	5	5	100	0	0
arrest in growth of kidney cell lines	3.528E-8	2	5	5	100	0	0
arrest in G1/S phase transition of fibroblasts	5.292E-8	2	5	5	100	0	0
arrest in G1/S phase transition of connective tissue	7.409E-8	2	5	5	100	0	0
G1/S phase transition of embryonic cell lines	7.409E-8	2	5	5	100	0	0
arrest in cell cycle progression of breast cell lines	9.878E-8	2	5	5	100	0	0
senescence of epidermal cells	9.878E-8	2	5	5	100	0	0
senescence of dermal cells	1.588E-7	2	5	5	100	0	0
cytostasis of epidermal cells	1.588E-7	2	5	5	100	0	0
cytostasis of dermal cells	1.588E-7	2	5	5	100	0	0

SIFT Function Prediction : Damaging
 PolyPhen-2 Function : Benign

Legend [show]

Can add it to your current fastq->vcf pipeline



- Identify 'short' list of most plausible variants
 - Causal
 - Biomarkers
- Construct mechanistic hypothesis based on supported biological relationships
- Share with colleagues/ potential collaborators

Navigation Area

- Sibling reads Chr14
- Mother reads Chr14
- Affected Child Only
 - Affected child reads Chr14
 - Affected Child Vars-WF 10.23
 - Affected child reads Chr14 Read Mapping
 - Affected child reads Chr14 Target Region Coverage
 - Affected child reads Chr14 Target Region Coverage

Search: <enter search term>

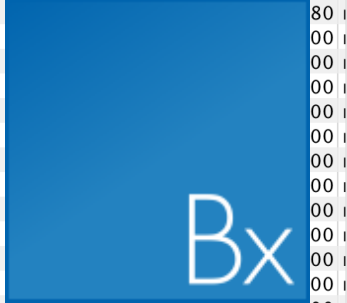
Toolbox

- InDels and Structural Variants
- Whole Genome Coverage Analysis
- Variant Detectors
- Add Information to Variants
- Remove Variants
- Add Information to Genes
- Compare Samples
- Ingenuity Pathway Analysis
- Ingenuity Variant Analysis**
- Ingenuity Variant Analysis**
- Ingenuity Variant Analysis for Hereditary Diseases**
- Ingenuity Variant Analysis for Hereditary Diseases

* Copy of Ident... x Affected chil... x

Rows: 1,118 Table view: Homo sapiens Filter

Type	Reference	Allele	Reference al...	Length	Zygoty	Coverage	Frequency	Probability
SNV	A	G	No		1 Heterozygous	182	40.66	1.00
SNV	A	A	Yes		1 Heterozygous	182	59.34	1.00
SNV	C	T	No		1 Heterozygous	160	23.75	1.00
SNV	C	C	Yes		1 Heterozygous	160	76.25	1.00
SNV	G	A	No		1 Heterozygous	162	23.46	1.00
SNV	G	G	Yes		1 Heterozygous	162	76.54	1.00
SNV	A	G	No		1 Heterozygous	58	20.69	0.80
SNV	A	A	Yes		1 Heterozygous			80
SNV	A	G	No		1 Heterozygous			00
SNV	A	A	Yes		1 Heterozygous			00
SNV	A	G	No		1 Heterozygous			00
SNV	A	A	Yes		1 Heterozygous			00
SNV	A	C	No		1 Heterozygous			00
SNV	A	A	Yes		1 Heterozygous			00
SNV	A	C	No		1 Heterozygous			00
SNV	A	A	Yes		1 Heterozygous			00
Deletion	A	-	No		1 Heterozygous			00
SNV	A	A	Yes		1 Heterozygous			00
SNV	C	T	No		1 Heterozygous			00
SNV	C	C	Yes		1 Heterozygous			00
SNV	A	G	No		1 Heterozygous			00
SNV	A	A	Yes		1 Heterozygous	158	74.68	1.00
	C	No			1 Heterozygous	312	64.74	1.00
	T	Yes			1 Heterozygous	312	35.26	1.00
	G	No			1 Heterozygous	296	68.92	1.00
	C	Yes			1 Heterozygous	296	31.08	1.00
	T	No			1 Heterozygous	718	21.73	0.62
	C	Yes			1 Heterozygous	718	78.27	0.62
	T	No			1 Heterozygous	400	24.00	1.00
	C	Yes			1 Heterozygous	400	76.00	1.00
	SNV	G	No		1 Heterozygous	414	25.60	1.00
	SNV	C	Yes		1 Heterozygous	414	74.40	1.00



Ingenuity Variant Analysis for Hereditary Diseases

1. Choose where to run

2. Select variant track for proband

Select variant track for proband

Navigation Area

- ▶ S. cerevisiae References
- ▶ bam files

Selected elements (1)

- ▶ Affected Child Identified Variants

Ingenuity Variant Analysis for Hereditary Diseases

1. Choose where to run

2. Select variant track for proband

3. Variant analysis parameters

Variant analysis parameters

Analysis configuration

Reference Homo_sapiens_sequence_hg19

Variant Analysis Genetic Disease Pipeline

Variant Analysis Custom Pipeline/specify analysis name

Upload only

Disease inheritance pattern This disease is caused by a de novo mutation

Custom analysis name

Naming

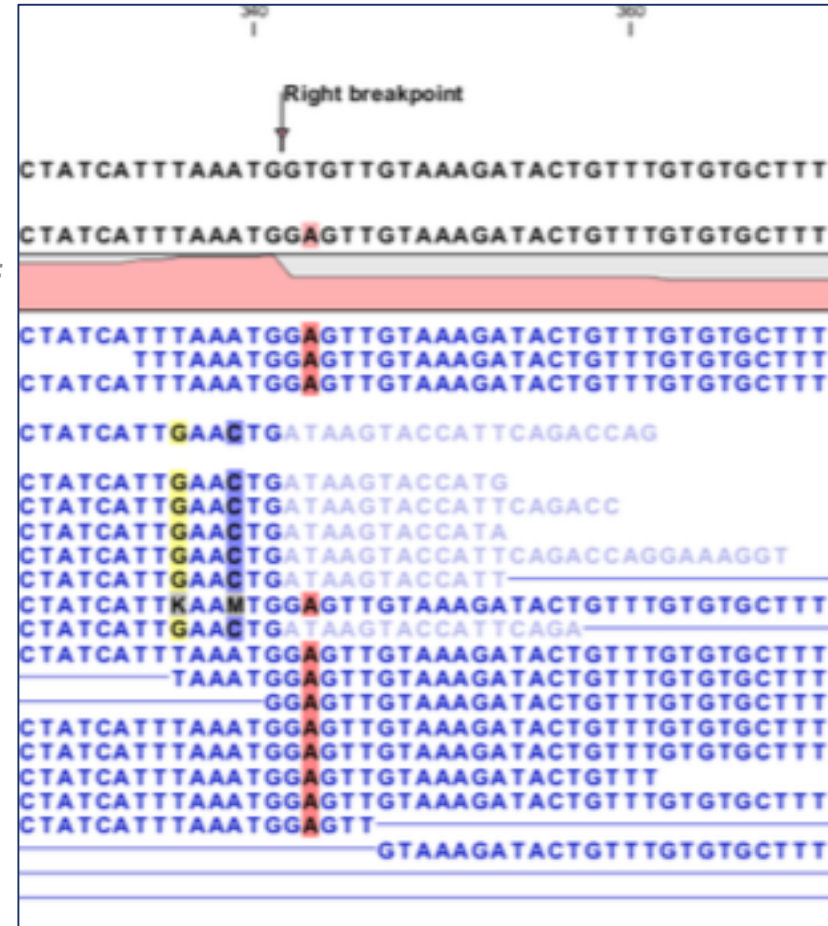
Analysis name

Analysis description {input};{date} Description

Press Shift + F1 for options

Previous
Next
Finish
Cancel

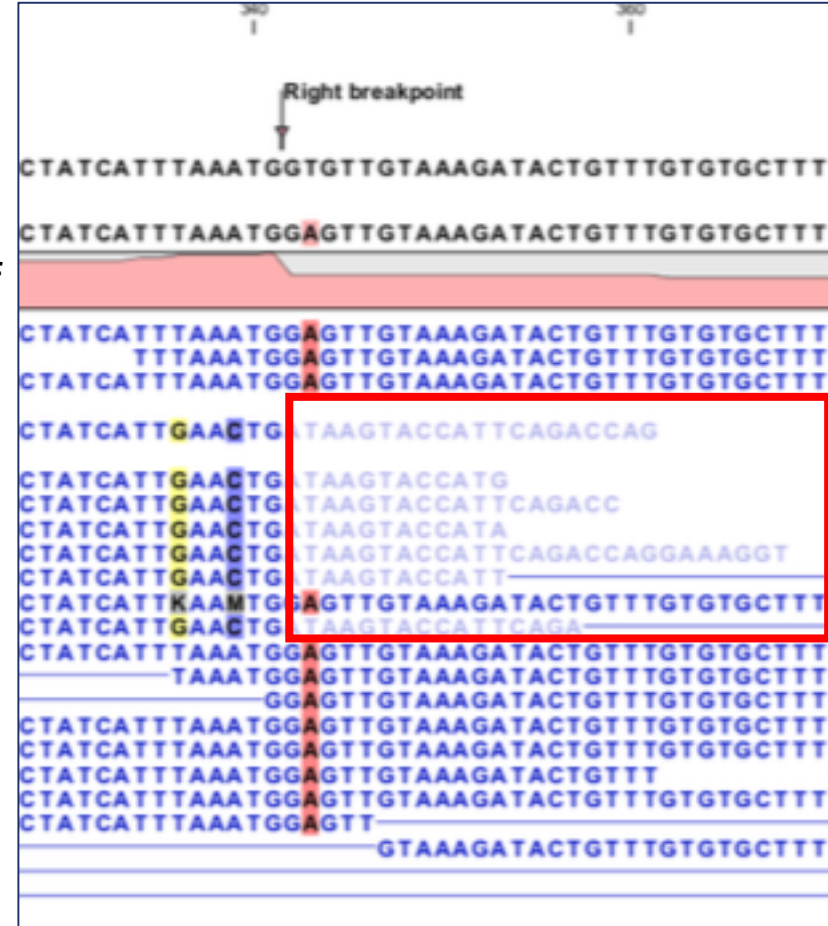
- Identify insertions, deletions [Indels], inversions, translocations and tandem duplications [Structural] from read mappings.
- Relies on unmapped read ends
- The Algorithm
 - First identifies positions with an excess of reads with left (or right) unaligned ends.
 - Determines consensus sequences of the unaligned ends
 - Maps the consensus sequences to the reference sequence around other positions with unaligned ends.
 - Structural variant is called when mappings are in accordance with a 'signature' of a structural variant.



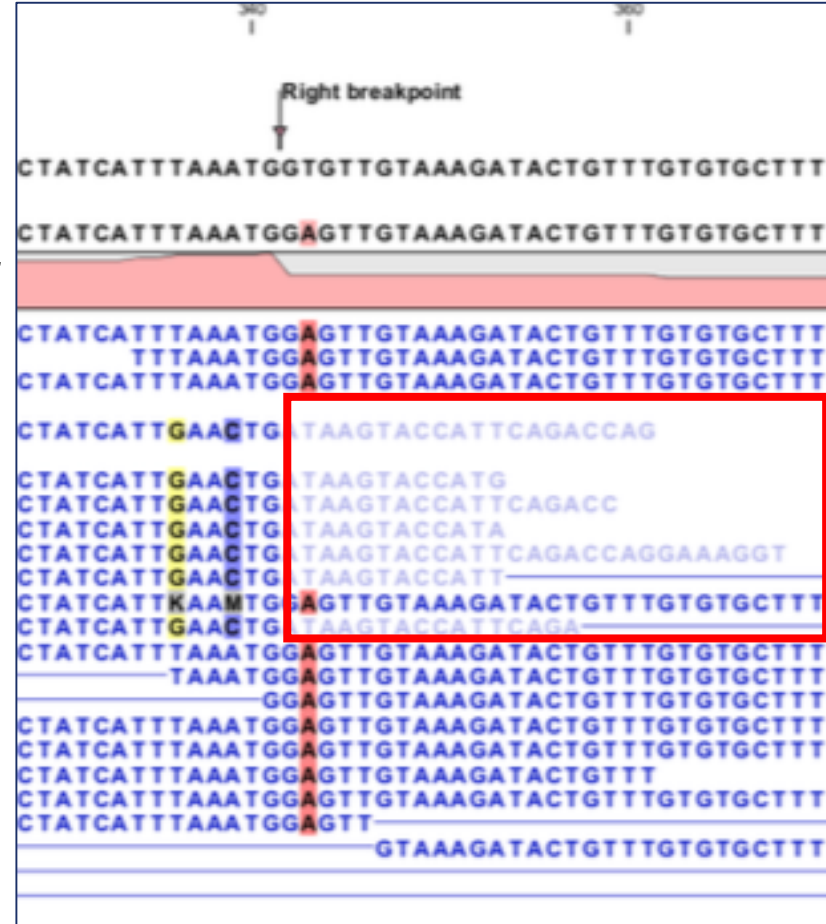
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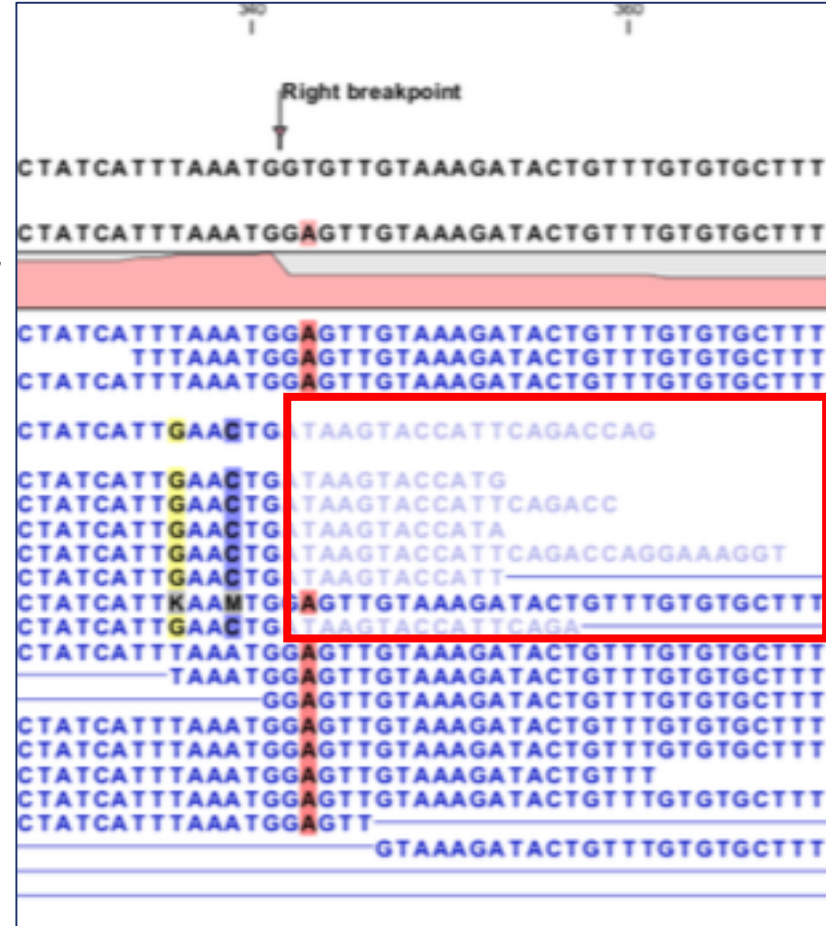
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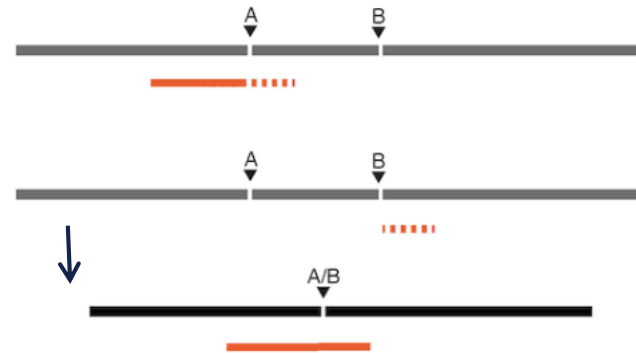
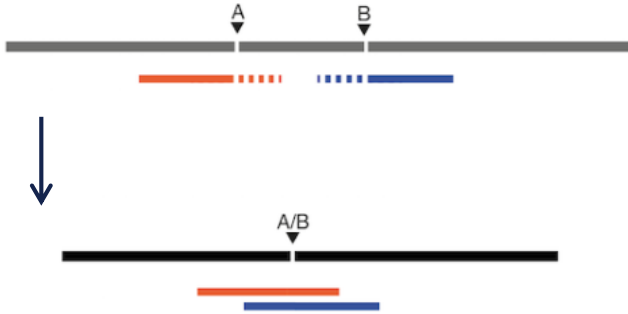




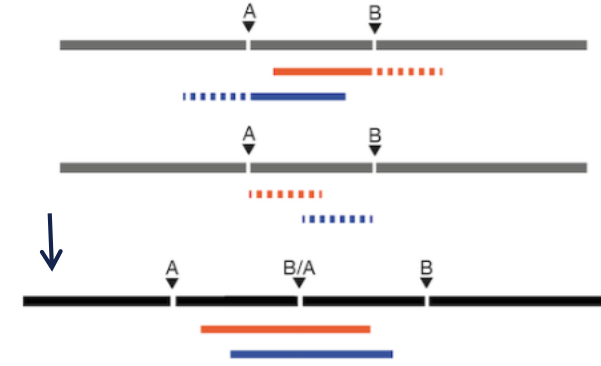
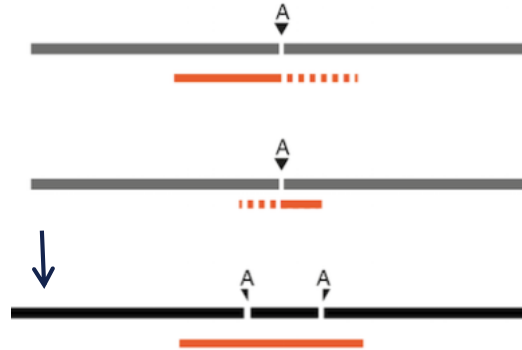
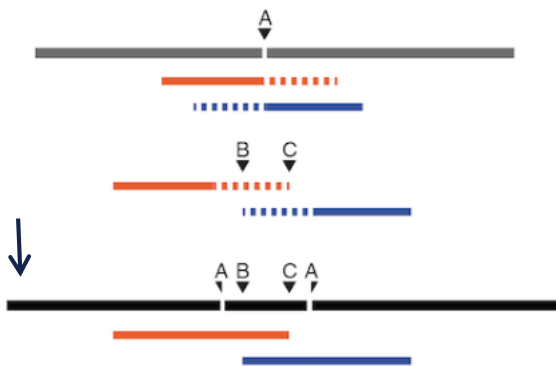
Indel and Structural Variants- The Algorithm

Structural variant signatures:

Deletions: Unaligned sequence in between breakpoints



Insertions: Unaligned sequence on either side of a breakpoint

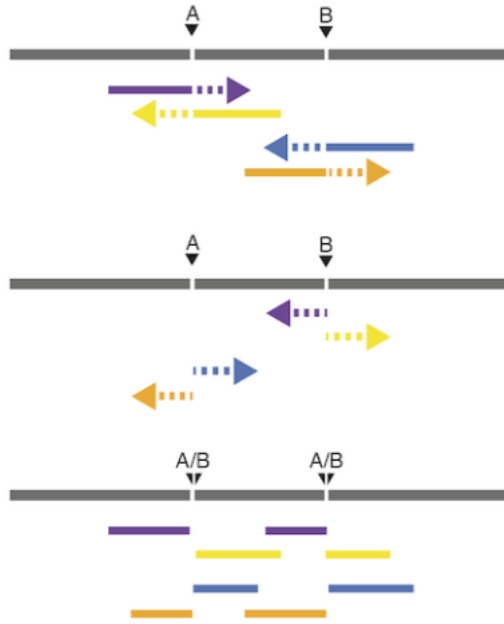




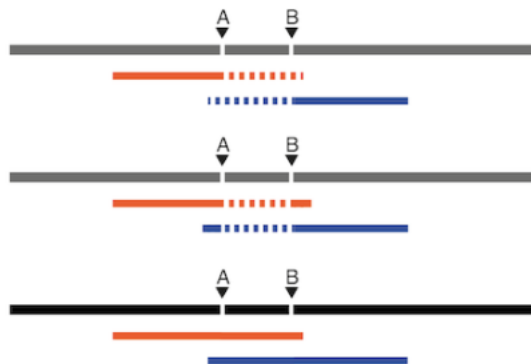
Indel and Structural Variants- The Algorithm

Structural variant signatures:

Inversions



Replacement



Translocation: Deletion of SeqY between breakpoints A and B and insertion of SeqY at C.

