

Note

Since we conducted the interviews in German language, these slides were translated for this publication.



1. SOPHiA GENETICS

Online platform for analysis of high-throughput sequencing data and clinical interpretation of variants. It is also possible to share the evaluation of variants with other institutions.

SNV/INDELs

WORKSPACE

Requests

ANAL... BRCA

ANALYSIS

K01_S1_L001_R1_001.fastq.gz

BRCA

S15 - -

BRCA

2 genes

Patient's Disease (0)

OVERVIEW

SCREENING

GENES

SNVs/INDELs

CNVs

WARNINGS

Sophia Filters

Retained Variants

24

Highly Pathogenic

A

4

Potentially Patho...

B

3

Unknown Signific...

C

10

Likely Benign

D

7

Low Confidence V...

9

Flagged Variants

10

Variant List - sorted by: PRED_CAT > PATHOGENICITY_CLASS > GENE

P	Pat.	i...	!	type	gene	cod. cons.	c.DNA	depth	VF%	ref	alt
A				INDEL	BRCA2	frameshift	c.6373dupA	797	50.6	GAAAA...	GAAAA...
B				SNP	BRCA1	missense	c.4956G>A	224	47.8	C	T
C	5			SNP	BRCA1	intronic	c.4987-68A>G	238	48.7	T	C
C	5			SNP	BRCA1	intronic	c.4485-63C>G	535	50.5	G	C
C	5			SNP	BRCA1	synonymous	c.2311T>C	338	53.0	A	G
C	4			SNP	BRCA1	synonymous	c.2082C>T	175	45.7	G	A
C	4			SNP	BRCA2	synonymous	c.4563A>G	686	99.7	A	G
C	3			SNP	BRCA2	synonymous	c.6513G>C	200	100.0	G	C
C	2			SNP	BRCA1	missense	c.3113A>G	692	44.4	T	C
C	1			SNP	BRCA1	intronic	c.5152+66G>A	292	45.2	C	T
C	1			SNP	BRCA2	intronic	c.7806-14T>C	574	48.8	T	C

OVERVIEW

DETAILS

FLAGGING

VIEWER

SIMILAR PATIENTS

WARNINGS

reads

224

DEPTH

175 min

883 max

frequencies

1/8

RUN

7%

ACCOUNT

3.5%

flagging

16 9

1 2 3 4 5

D C B A

Add To Rep...

0

transcript

NM_007294

cDNA

c.4956G>A

ref/alt

C→T

sequence

ATG→ATA

amino acid

M→I

protein

p.Met1652Ile

strand

<<<

rs number

SNP

31

16-15

missense

Requests

samples:8

BRCA

Samples


 report

level	count
low	5
medium	2
rejected	1

40282-197-S17 

40283-198-S31 

40277-192-S8 

amplicon: BRCA1_ex19_01 - confidence: HIGH - plex 2

Sample: 40282-197-S17

CN (copy number)

Amplicons

Amplicon	CN (copy number)
BRCA1_ex24_01	1.9
BRCA1_ex23_01	1.8
BRCA1_ex22_01	2.0
BRCA1_ex21_01	2.0
BRCA1_ex19_01	1.9
BRCA1_ex18_01	2.0
BRCA1_ex17_01	2.0
BRCA1_ex16_01	2.0
BRCA1_ex16_02	2.0
BRCA1_ex15_01	1.7
BRCA1_ex14_01	2.0
BRCA1_ex13_01	1.9
BRCA1_ex12_01	1.9
BRCA1_ex11_01	1.9
BRCA1_ex11_02	1.9
BRCA1_ex11_03	1.9
BRCA1_ex11_04	1.8
BRCA1_ex11_05	2.0
BRCA1_ex11_06	1.9
BRCA1_ex11_07	2.3
BRCA1_ex11_08	1.9
BRCA1_ex11_09	1.5
BRCA1_ex11_10	1.9
BRCA1_ex11_11	2.0
BRCA1_ex11_12	2.0
BRCA1_ex11_13	2.0
BRCA1_ex11_14	2.0
BRCA1_ex10_01	2.0
BRCA1_ex09_01	1.8
BRCA1_ex08_01	1.8
BRCA1_ex07_01	1.0
BRCA1_ex06_01	1.1
BRCA1_ex05_01	1.1
BRCA1_ex03_01	1.0
BRCA1_ex02_01	0.9

Variants Report



Variant Report

Patient

First name:
Last name:
Patient ID: **SG10000002**
DOB: **2 Jan 1967**
Gender: **Female**
Father ethnicity: -- Unknown --
Mother ethnicity: -- Unknown --

Analysis by



Analysis

Analysis ID: **40538**
MID: **S2**
Request run date:
Request run name: **HCS by Sophia**

RESULTS

SNVs/INDELs (selected in report)

Gene Transcript	Exon	c.DNA Protein alteration	Variant Fraction Coverage (ref / alt)	Coding consequence	Pathogenicity	ClinVar
<i>BRCA1</i> NM_007294	10	c.4065.4068delTCAA p.Asn1355Lysfs*10	47.3 % (785 / 709)	frameshift	Prediction A Highly Pathogenic	rs80357508
comment: The detected variant is highly pathogenic						

SNVs/INDELs (retained)

Gene Transcript	Exon	c.DNA Protein alteration	Variant Fraction Coverage (ref / alt)	Coding consequence	Pathogenicity	ClinVar
<i>ATM</i> NM_000051	3	c.146C>G p.Ser49Cys	51.7 % (1009 / 1081)	missense	Prediction B Potentially Pathogenic	rs1800054
<i>ATM</i> NM_000051	40	c.5948A>G p.Asn1983Ser	100.0 % (0 / 1750)	missense	Prediction C Unknown Significance	rs659243
<i>BARD1</i> NM_000465	1	c.70C>T p.Pro24Ser	48.75 % (818 / 778)	missense	Prediction C Unknown Significance	rs1048108
<i>BARD1</i> NM_000465	6	c.1518T>C p.= (p.His506His)	100.0 % (0 / 1753)	synonymous	Prediction C Unknown Significance	rs2070093

OncoPortal

1

T2
T4
D

EGFR-AS1
Missense mutation
VF: 50.38% depth: 2356

p.Thr790Met

Sensitive
Osimertinib mesylate
Therapeutic agent
Carcinoma, Non-Small-Cell Lung

Summary:
EGFR c.2369C>T is a missense mutation in codon 790 yielding a threonine-to-methionine (T790M) amino acid change (J Thorac Oncol 2013, 8(1): 45-51). EGFR is mutated in approximately 12% of non-small cell lung ...
Clinical Trial(s): 29

2

3

WORKSPACE
Requests

VIB
Variant Database Browser

ANALYSIS PM 001234
#3-0117

PROJECT
OncoPortal checking

SAMPLE
#89774 PM 0001234 < 1/6 >

RUN
23/05/2017

PM 0001234

Overview

Therapeutic

Diagnosis Prognosis

Variants

☒ Diseases
Carcinoma, Non-Sm...

☒ Gene
EGFR

☒ Drugs
EGFR (HER1; erbB1)...

Evidence Levels:

1/7

1/10

36 Clinical Associations

799 Clinical Trials

T2
T4
D

EGFR
Missense mutation
VF: 50.51% depth: 2548

p.Thr790Met

Sensitive
Osimertinib mesylate
Therapeutic agent
Carcinoma, Non-Small-Cell Lung

Summary:
EGFR c.2369C>T is a missense mutation in codon 790 yielding a threonine-to-methionine (T790M) amino acid change (J Thorac Oncol 2013, 8(1): 45-51). EGFR is mutated in approximately 12% of non-small cell lung ...
Clinical Trial(s): 29

T2
T4
D

EGFR
Missense mutation
VF: 50.51% depth: 2548

p.Thr790Met

Likely resistant
Erlotinib hydrochloride
Therapeutic agent
Carcinoma, Non-Small-Cell Lung

Summary:
no summary
Clinical Trial(s): 0

T2
T4
D

EGFR
Missense mutation
VF: 50.51% depth: 2548

p.Thr790Met

Resistant
Erlotinib hydrochloride
Therapeutic agent
Carcinoma, Non-Small-Cell Lung

Summary:
no summary
Clinical Trial(s): 37

T2
T4
D

EGFR
Missense mutation
VF: 50.51% depth: 2548

p.Thr790Met

Contradictory
EGFR (HER1; erbB1) Inhibitors
Mechanism of action
Carcinoma, Non-Small-Cell Lung

Summary:
EGFR c.2369C>T is a missense mutation in codon 790 yielding a threonine to methionine (T790M) amino acid change (J Thorac Oncol 2013, 8(1): 45-51). EGFR is mutated in approximately 12% of non-small cell lung ...
Clinical Trial(s): 0

T2
T4
D

EGFR
Missense mutation

p.Thr790Met

Likely resistant
Gefitinib

Summary:
no summary



2. CIViC

Cites from CIViC [homepage](#) & [nature paper](#):

- "CIViC is an **open access, open source**, community-driven web resource for Clinical Interpretation of Variants in Cancer."
- "CIViC is an **expert-crowdsourced knowledgebase** for Clinical Interpretation of Variants in Cancer describing the therapeutic, prognostic, diagnostic and predisposing relevance of inherited and somatic variants of all types"

CIViC

AboutParticipateCommunityHelpFAQSign In/Sign Up

Go to Genes & VariantsGo!

BROWSE

SEARCH

ACTIVITY

ADD

GENE BRAF

Gene SummaryGene Talk

BRAF mutations are found to be recurrent in many cancer types. Of these, the mutation of valine 600 to glutamic acid (V600E) is the most prevalent. V600E has been determined to be an activating mutation, and cells that harbor it, along with other V600 mutations are sensitive to the BRAF inhibitor dabrafenib. It is also common to use MEK inhibition as a substitute for BRAF inhibitors, and the MEK inhibitor trametinib has seen some success in BRAF mutant melanomas. BRAF mutations have also been correlated with poor prognosis in many cancer types, although there is at least one study that questions this conclusion in papillary thyroid cancer.

Sources:

Li et al., 2009, Oncol. Rep.

Pakneshan et al., 2013, Pathology

Name:

B-Raf proto-oncogene, serine/threonine kinase

Entrez Symbol:

BRAF

Entrez ID:

673

Aliases:

B-RAF1, B-raf, BRAF1, NS7, RAFB1

Chromosome:

7

Start:

140419127

End:

140624564

Strand:

-1

(GRCh37)

Protein Domains:

Diacylglycerol/phorbol-ester binding, Protein kinase C-like, phorbol ester/diacylglycerol-binding domain, Protein kinase domain, Protein kinase, ATP binding site, Protein kinase-like domain... (5 more)

Pathways:

EGFR1, Downstream signaling in naïve CD8+ T cells, CDC42 signaling events, ErbB1 downstream signaling, Signaling events mediated by focal adhesion kinase... (139 more)

View MyGene.info Details

MyGene.info

BRAF Variants & Variant Groups

Show all:filter variants...

599INST

AGK-BRAF

AKAP9-BRAF

AMPLIFICATION

BRAF-CUL1

CUX1-BRAF Fusion

D594A

D594G

D594N

D594V

DEL 485-490

DELNVTAP

F595L

G464V

G466A

G466V

G469A

G469E

G469R

G469V

G496A

G596C

G596R

G596V

G606E

intron 10 rearrangement

intron 9 rearrangement

K483M

K601E

KIAA1549-BRAF

L505H

L597Q

L597R

L597S

L597V

MACF1-BRAF Fusion

MUTATION

N581S

P731T

PAPSS1-BRAF

PPFIBP2-BRAF

TRIM24-BRAF

V600

V600_K601DELINS

V600D

V600E

V600E AMPLIFICATION

V600E+V600M

V600K

V600R

WASFL-BRAF Fusion

WILD TYPE

ZKSCAN1-BRAF

Other V600's Group

L597R

V600

V600D

BRAF Fusions Group

AGK-BRAF

AKAP9-BRAF

BRAF-CUL1

Kinase Dead BRAF Mutation Group

D594A

D594V

K483M

VARIANT V600D

Variant Summary

Variant Talk

Last Modified by

CIViC_Bot

Last Reviewed by

ahwagner

Last Commented On by

ahwagner

Aliases: RS121913377 and VAL600ASP

Allele Registry ID: CA457986948

Patients harboring mutations in valine 600 residue of BRAF have been shown to be sensitive to dabrafenib. For more information on the V600 locus, see the V600E entry.

Variant Type:
Missense Variant

HGVS Expressions:

NC_000007.13:g.140453135_140453136delinsAT ,
NM_004333.4:c.1799_1800delTGinsAT ,
NP_004324.2:p.Val600Asp ,
ENST00000288602.6:c.1799_1800delTGinsAT , and
NC_000007.13:g.140453135_140453136delinsTA

ClinVar ID:
375939

CIViC Actionability Score:
25

Ref. Build: GRCh37 Ensembl Version: 75

Chr.	Start	Stop	Ref. s	Var. Bases
7	140453135	140453136	CA	TA

Rep. Transcript
ENST00000288602.6

ClinVar ID

ClinVar Clinical Significance

—

—

COSMIC ID

dbSNP RSID

HGVS ID

—

—

chr7:g.140453135_140...

SnpEff Effect

SnpEff Impact

gnomAD Adj. AF

synonymous variant

LOW

—

View MyVariant.info Details

MyVariant.info

Evidence for V600D 3 total items





Get Data

Help

EID	DESC	DIS	DRUGS	EL	ET	ED	CS	VO	TR	
94	Patients with other BRAF V60...	Melanoma	Dabrafenib	B					5 ★	
4489	In an in vitro study, the WM26...	Melanoma	Vemurafenib	D						
4488	In an in vitro study, WM2664, ...	Melanoma	Vemurafenib	D						

Column Abbreviation Column Description

EID Evidence ID Number






-  Submitted
-  Accepted
-  Rejected
-  Has pending revisions

DESC Evidence Description





DIS Disease

DRUG Drug(s)

EL Evidence Level



-  Validated
-  Clinical
-  Case Study
-  Preclinical
-  Inferential

ET Evidence Type















-  Predictive
-  Diagnostic
-  Prognostic
-  Predisposing

Column Abbreviation Column Description





ED Evidence Direction

-  Supports
-  Does Not Support

CS Clinical Significance

-  Sensitivity/Response
-  Resistance
-  Better Outcome
-  Poor Outcome
-  Positive
-  Negative
-  Adverse Response
-  Reduced Sensitivity
-  Pathogenic
-  Likely Pathogenic
-  Benign
-  Likely Benign
-  Uncertain Significance
-  N/A

VO Variant Origin

-  Germline Mutation
-  Somatic Mutation
-  Germline Polymorphism
-  Unknown



3. Clarivate

MetaCore[®] / Key Pathway Advisor[®]

commercial product
just for comparison with industrial products
no replacement for cBioPortal

Übersicht MetaCore

Start Page


Applications ▾

Help ▾

User: deborahriley ▾

Search

Advanced Search



CFTR

Network object


 [Build Network](#)

Table of Contents

General

Gene Details

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Thomson Reuters Integrity

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Grouping Variants

Pathways and Processes

Diseases

Reactions

Interactions













Human

Mouse

Rat

▼ Gene Details

CFTR

Symbols	CFTR, ABC35, ABCC7, CF, CFTR/MRP, dJ760C5.1, MRP7, TNR-CFTR
Full Name	cystic fibrosis transmembrane conductance regulator
Synonyms	cystic fibrosis transmembrane conductance regulator, cystic fibrosis transmembrane conductance regulator (ATP-binding cassette sub-family C, member 7), cAMP-dependent chloride channel, channel conductance-controlling ATPase
Description	This gene encodes a member of the ATP-binding cassette (ABC) transporter superfamily. ABC proteins transport various molecules across extra- and intra-cellular membranes. ABC genes are divided into seven distinct subfamilies (ABC1, MDR/TAP, MRP, ALD, OABP, GCN20, White). This protein is a member of the MRP subfamily that is involved in multi-drug resistance. The encoded protein functions as a chloride channel and controls the regulation of other transport pathways. Mutations in this gene are associated with the autosomal recessive disorders cystic fibrosis and congenital bilateral aplasia of the vas deferens. Alternatively spliced transcript variants have been described, many of which result from mutations in this gene. [provided by RefSeq, Jul 2008]
Chromosomal Location	 Chr7 7q31.2
Predicted Target of microRNA by TargetScan	 CFTR
Species	 Homo sapiens
Orthologs (Homologenes, NCBI)	 Canis lupus familiaris ,  Danio rerio ,  Macaca mulatta ,  Mus musculus ,  Rattus norvegicus ,  Gallus gallus ,  Bos taurus ,  Pan troglodytes ,  Xenopus tropicalis

▼ Protein Details

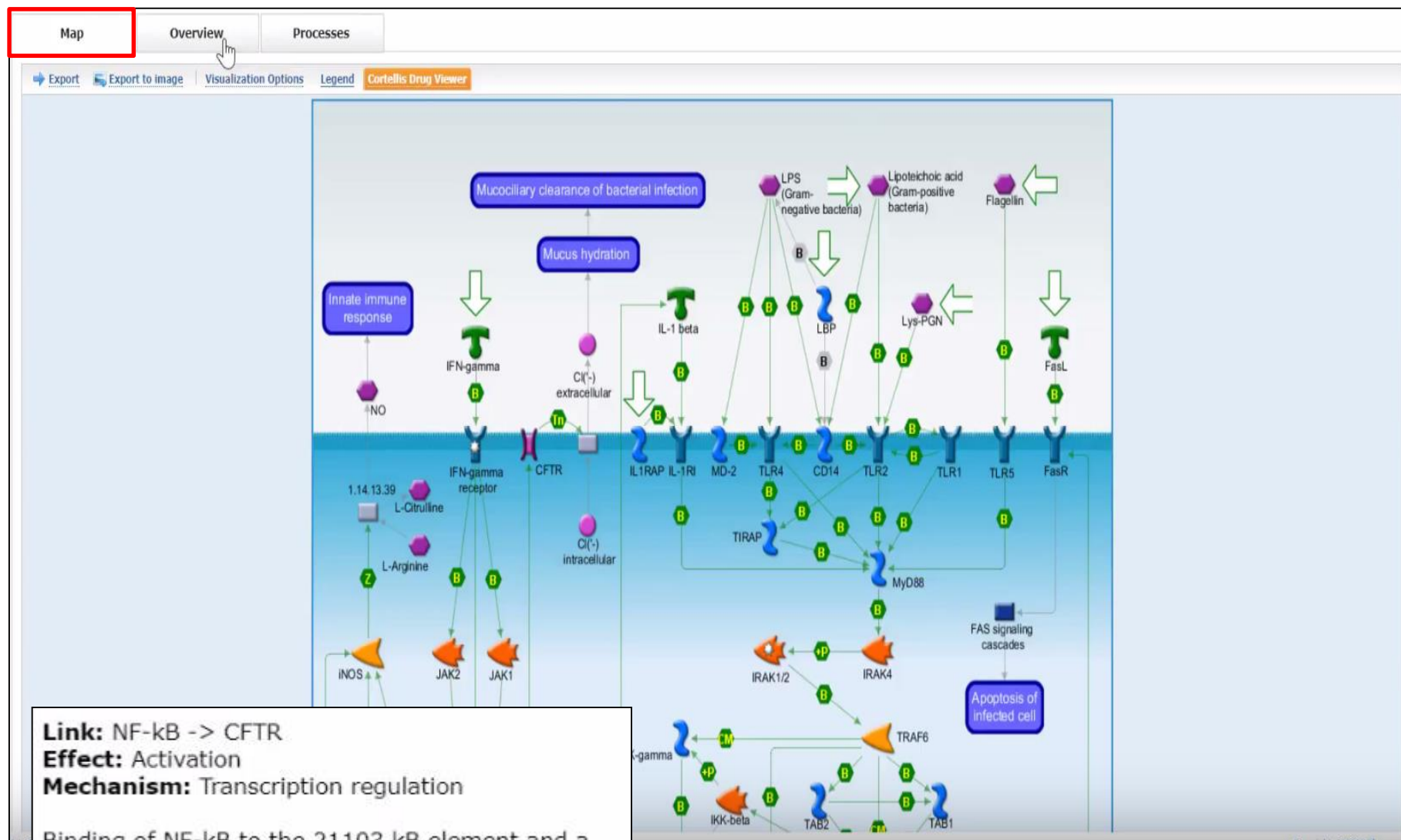
CFTR_HUMAN

Name	CFTR_HUMAN / Cystic fibrosis transmembrane conductance regulator
------	--

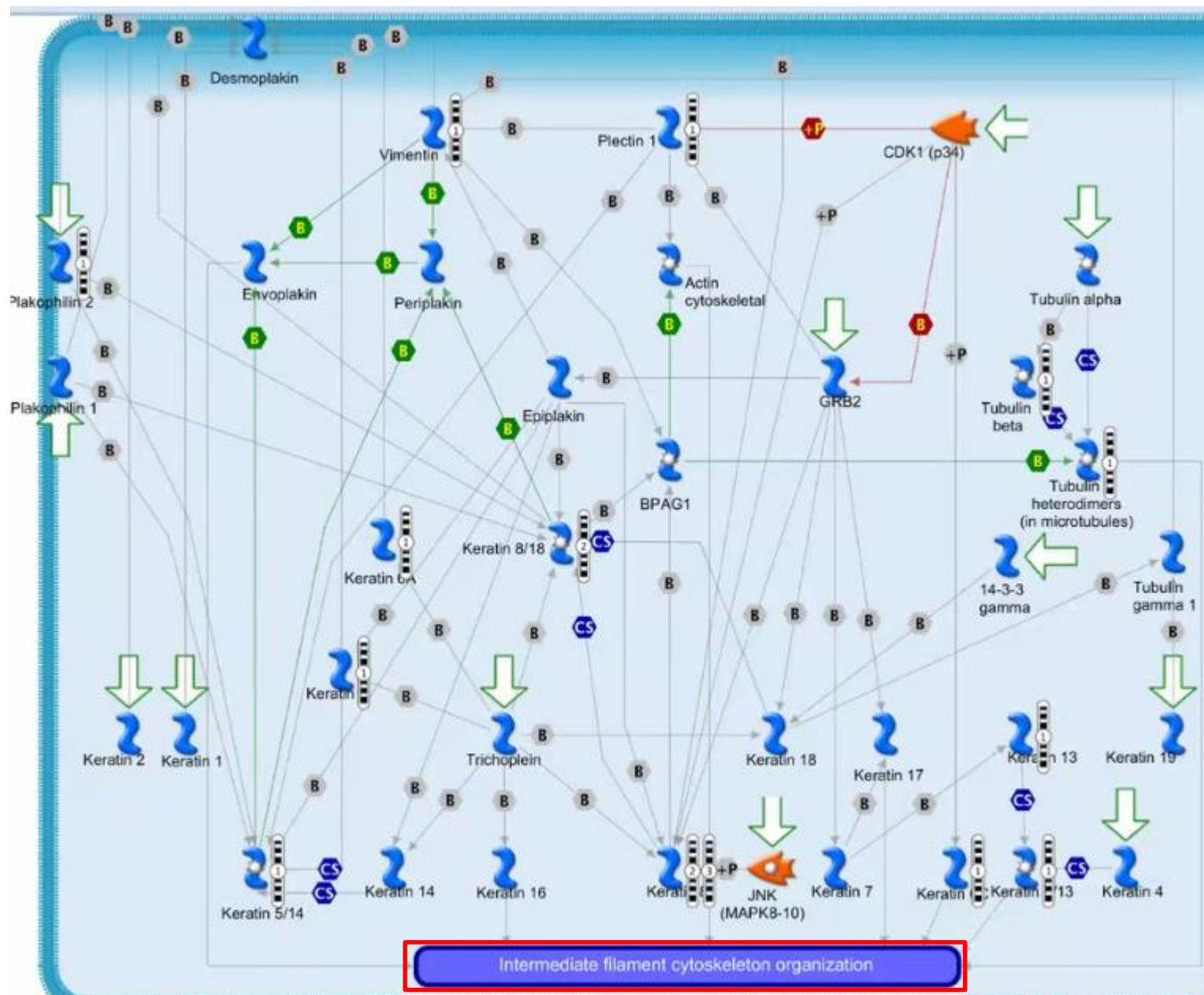
MetaCore+MetaDrug™ version 6.33 build 69110

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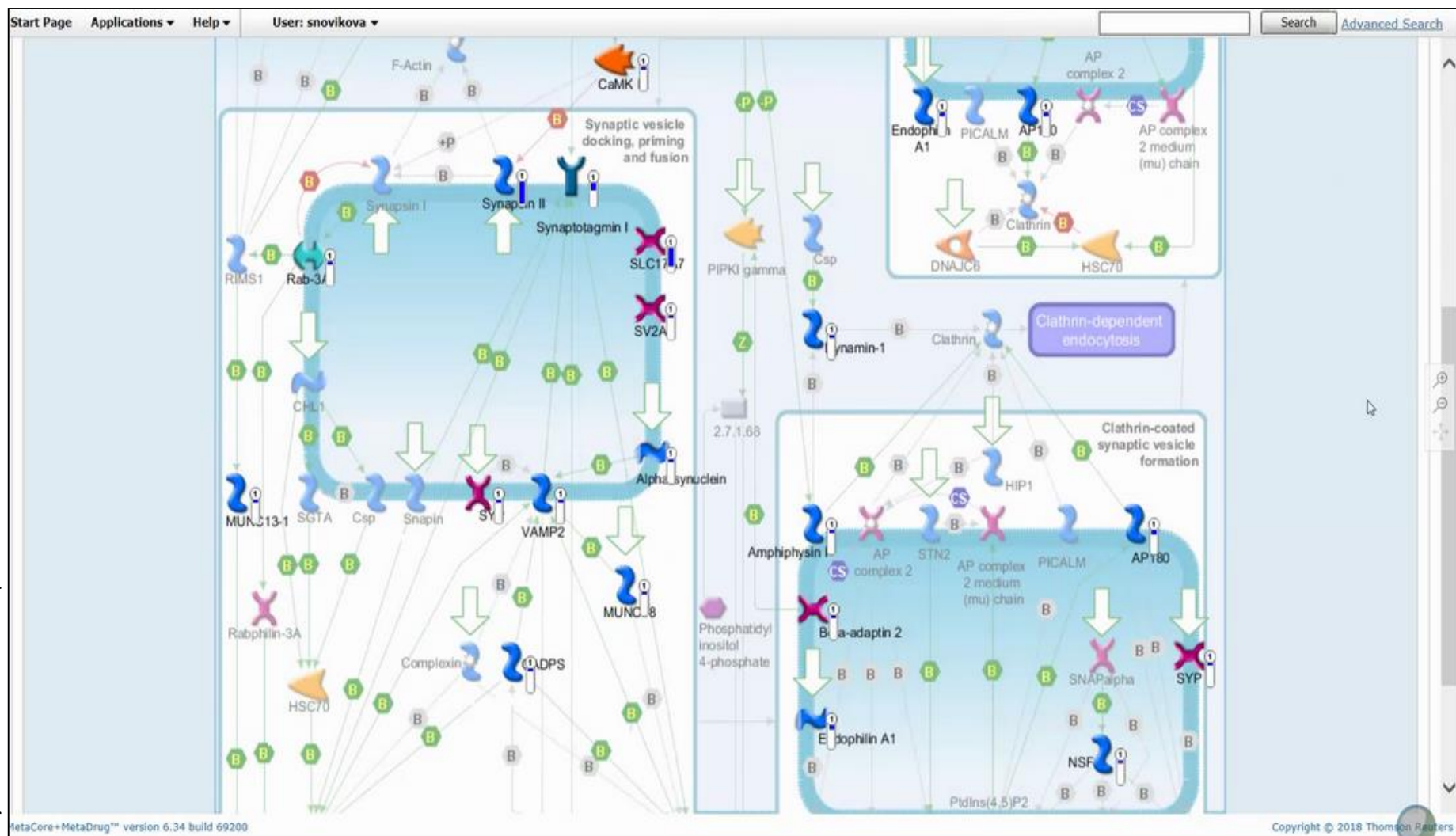
MetaCore: Map 1



MetaCore: Map 2



MetaCore: Map 3



Übersicht MetaCore

[Start Page](#) [Applications ▾](#) [Help ▾](#) [User: snovikova ▾](#) [Search](#) [Advanced Search](#)

[Map](#) [Overview](#) [Processes](#)

Keratin filaments

Cytoskeleton in most eukaryotic cells consists of three distinct, yet interconnected, filament systems: **Actin** filaments, **Microtubules** and intermediate filaments. Cell assembly is integrated by the network of intermediate filaments (IFs) and by their interactions with other cytoskeleton structural elements defining cytoarchitecture and cytodynamics.

IF network is critically involved in cell shape control and imparts intracellular mechanical strength. The family of IF proteins has five sub-families. Four of the sub-families are localized in the cytoplasm, whereas the fifth sub-family is found in the nucleus. Expression patterns of cytoplasmic IFs are cell- and tissue-type specific.

The main IF protein is found in epithelial cells is **Keratin** and in fibroblasts it is **Vimentin**. **Keratin** IFs are obligate co-polymers of acidic and basic cytokeratins [1], [2].

IF networks are cross-linked by special binding proteins, e.g., **Plectin**, **BPAG1**, **Desmoplakin**, **Envoplakin**, **Periplakin**, **Epiplakin**, **Trichoplein** and **Plakophilins** [3], [4], [5], [6]. These proteins maintain cell and tissue integrity by coordinated interconnection of three distinct cytoskeletal filament systems, and anchoring them to membrane complexes.

Assembly, disassembly and subcellular organization of IFs is regulated by kinases, e.g., by Mitogen-activated protein kinases 8-10 (**JNK(MAPK8-10)**) and Cell division cycle 2(**CDK1**) [7], [8].

Objects list:

14-3-3 gamma	14-3-3 protein gamma
Actin cytoskeletal	Actin cytoskeletal <i>Protein group</i>
BPAG1	Dystonin
CDK1 (p34)	Cyclin-dependent kinase 1
Desmoplakin	Desmoplakin
Envoplakin	Envoplakin
Epiplakin	Epiplakin
GRB2	Growth factor receptor-bound protein 2
JNK(MAPK8-10)	c-Jun N-terminal kinases <i>Protein group</i>
Keratin 1	Keratin, type II cytoskeletal 1
Keratin 13	Keratin, type I cytoskeletal 13
Keratin 14	Keratin, type I cytoskeletal 14
Keratin 16	Keratin, type I cytoskeletal 16

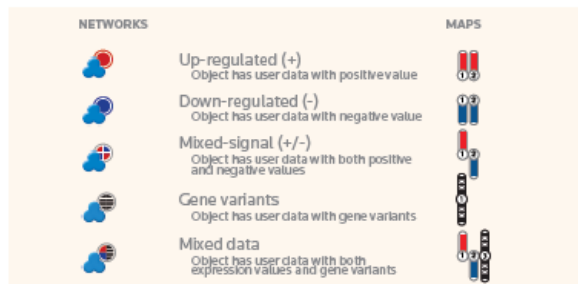
MetaCore+MetaDrug™ version 6.34 build 69200

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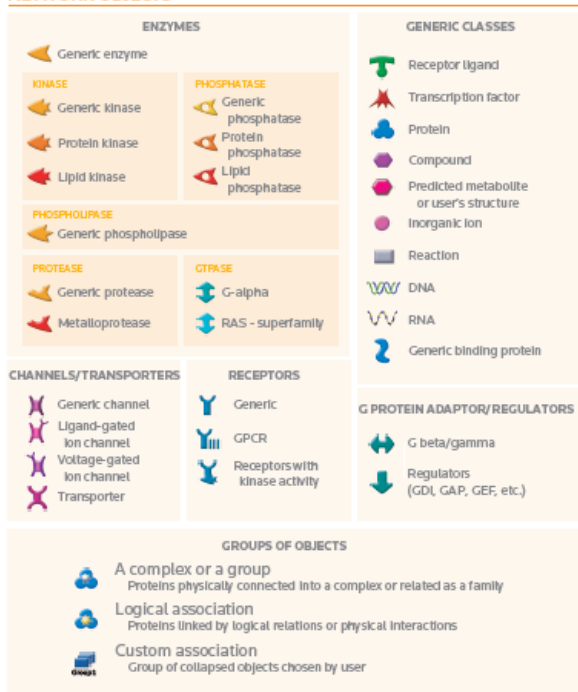
MetaCore: Legende

METACORE QUICK REFERENCE GUIDE

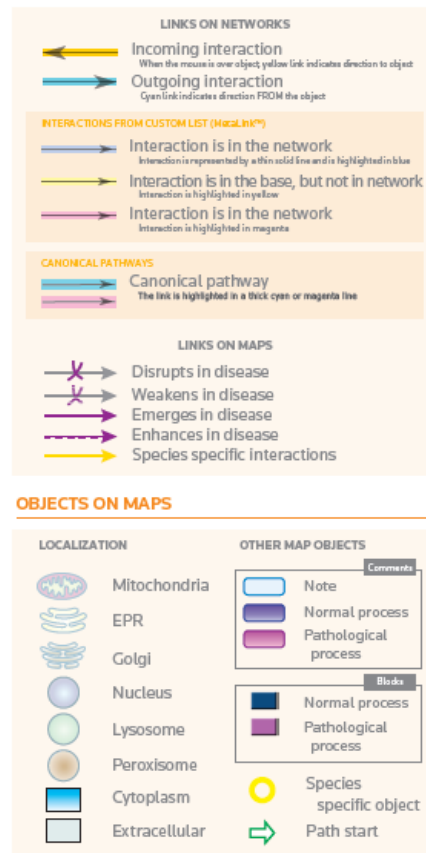
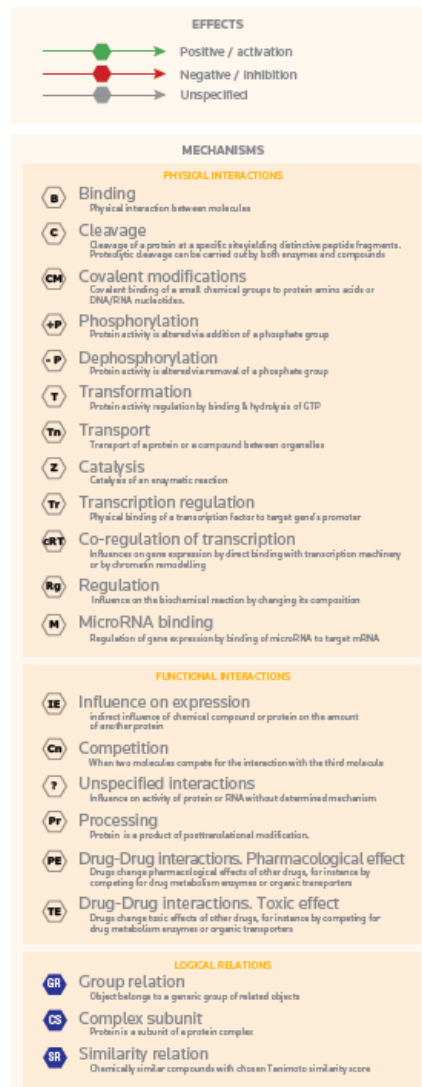
USER DATA



NETWORK OBJECTS



INTERACTIONS BETWEEN OBJECTS



THOMSON REUTERS REGIONAL OFFICES

North America

Philadelphia
+1 800 336 4474
+1 215 386 0100

Latin America

+55 11 8370 9845

Europe, Middle East and Africa

Barcelona +34 93 459 2220
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Asia Pacific

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LS0312

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THOMSON REUTERS™

Powerful analytics – causal reasoning

KEY HUBS

 Activated or Overconnected object
  Inhibited object

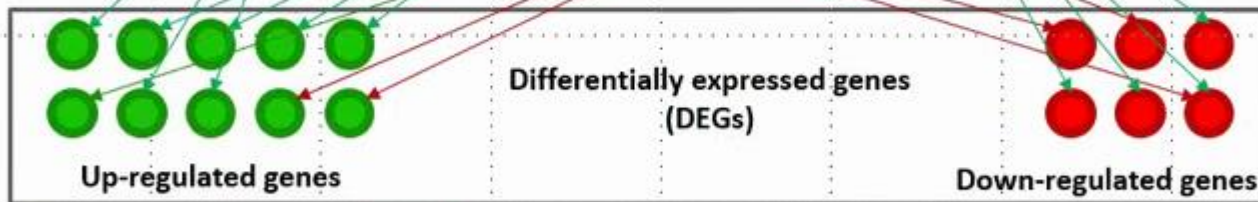
Identify the other proteins which regulate Transcription Factors



Predict Key Hubs on molecular network which drive differential expression

Predict active or inhibited Transcription Factors which change expression of genes

Active

Inhibited



 Documented inhibitory interaction
 Documented activatory interaction

Up-stream analysis

- Chindelevitch L, Ziemek D, Enayetallah A, Randhawa R, Sidders B, et al. (2012) Causal reasoning on biological networks: interpreting transcriptional changes. *Bioinformatics* 28: 1114-1121.
- Pollard J Jr, Butte AJ, Hoberman S, Joshi M, Levy J, Pappo J. (2005) A computational model to define the molecular causes of type 2 diabetes mellitus. *Diabetes Technol Ther*. 2005 Apr;7(2):323-36.

Key Pathway Advisor: Entities <-> Interactions

KEY PATHWAY ADVISOR

GSE18105_colon cancer vs norm / CDK4 - Step 3

?

🔊

📄

Key Hub

Table View

Tutorial

Molecular Entities

Filters (1)

Name	Your Data	Hypothesis Basis	Steps	Putative Biomarkers	Drug Targets	View Interactions
CDK4	▲ 4.22		▲		✓	→
E2F4			1		-	→
FOXO1			1		-	→
p130	▲ 3.84		1		-	→
p21	▼ -3.56		1		-	→
Rb protein			1		-	→
RUNX3			1		-	→
ABCG2	▼ -24.75	Incorrect	2		✓	→
Angiotensinogen	▲ 5.08	Incorrect	2		-	→
Aurora-A	▲ 6.61	Correct	2		✓	→
Aurora-B	▲ 5.08	Correct	2		✓	→
Axin2	▲ 3.33	Correct	2		-	→
Beta-2 adrenergic receptor	▼ -3.77	Correct	2		-	→

Interactions

Filters (0)

FROM	Mechanism	TO
AP-2A	Transcription regulation	BET1-IG-H3
AP-2A	Transcription regulation	UNG2
Bcl-6	Transcription regulation	TCF7 (TCF1)
c-Myc	Transcription regulation	ACP1
c-Myc	Transcription regulation	Adenylate cyclase type III
c-Myc	Transcription regulation	ATP8A1
c-Myc	Transcription regulation	AXUD1
c-Myc	Transcription regulation	BXDC1
c-Myc	Transcription regulation	C1TM
c-Myc	Transcription regulation	CGI-30
c-Myc	Transcription regulation	CLN6
c-Myc	Transcription regulation	CSE1L
c-Myc	Transcription regulation	Cyclin J
c-Myc	Transcription regulation	DOCK10

Key Pathway Advisor: Putative Biomarkers

KEY PATHWAY ADVISOR GSE18105_colon cancer vs norm / CDK4 - Step 3

Key Hub Table View Tutorial

Molecular Entities

Filters (1)

Name	Your Data	Hypothesis Basis	Steps	Putative Biomarkers	Drug Targets	View Interactions
CDK4	4.22			Perfect	✓	→
Anus Neoplasms		(Ac) Activity		Perfect		→
Protein		(Ab) Abundance				→
CDN1A_HUMAN	▼ Ab			Anal Canal	View	→
Colonic Neoplasms		(Ac) Activity		Perfect		→
Protein		(Ab) Abundance				→
CDN1A_HUMAN	▼ Ab			Intestinal Mucosa	View	→
Colorectal Neoplasms		(Ac) Activity		Perfect		→
Protein		(Ab) Abundance				→
CDKN1A_(HUMAN)_transcript	▼ Ab			Intestine, Large	View	→

View Biomarker

Interactions

Filters (0)

FROM	Mechanism	TO
AP-2A	Transcription regulation	BETA-IG-H3
AP-2A	Transcription regulation	UNG2
Bcl-6	Transcription regulation	TCF7 (TCF1)
c-Myc	Transcription regulation	ACP1
c-Myc	Transcription regulation	Adenylate cyclase type III
c-Myc	Transcription regulation	ATP8A1
c-Myc	Transcription regulation	AXUD1
c-Myc	Transcription regulation	BXDC1
c-Myc	Transcription regulation	C1TM
c-Myc	Transcription regulation	CGI-30
c-Myc	Transcription regulation	CLN6
c-Myc	Transcription regulation	CSE1L
c-Myc	Transcription regulation	Cyclin J
c-Myc	Transcription regulation	DOCK10

Key Pathway Advisor: Putative Biomarkers

KEY PATHWAY ADVISOR

YOUR DATA

KEY HUBS

KEY PROCESSES

Pathway Maps

Pathological Pathway Maps

Physiological Pathway Maps

Diseases

Process Networks

Pathway Groups

DRUG TARGETS

Similar diseases

PUTATIVE BIOMARKERS

Similar diseases

ANALYSIS SETTINGS

GSE18105_colon cancer vs norm



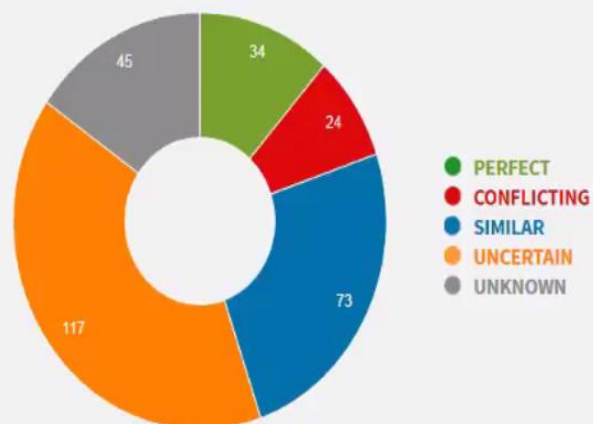
Download Report

293 PUTATIVE BIOMARKERS

This analysis compares the direction of your gene expression (or Key Hub activity) with known directional changes manually curated from literature within Key Pathway Advisor database. The database includes biomarker knowledge for DNA, RNA, Protein and post translational modifications levels. This table therefore allows you to understand how your experimental data aligns with current knowledge of these molecules in association with your chosen disease/indication.

How is this score assigned?

Biomarker match score



☒ Show only significantly associated (p-value<0.05) with pathology or prognosis.

Gene	Selected disease	Score	
ACP1	Colonic Neoplasms	PERFECT	+
ADAMTS1	Colonic Neoplasms	PERFECT	+
AGO1	Colonic Neoplasms	UNCERTAIN	+

Requirements Analysis and Specification for a Molecular Tumor Board Platform Based on cBioPortal (Buechner P. et al.)
Supplementary File 4: Presentation of potential tools



4. COMPASS™ for My Geisinger

WHOLE GENOME
SEQUENCING

Provider Report

Summary of Findings

Resources

SimulConsult Patient Summary

Lab Reports 1 +

Patient Report

Report Overview

Primary Findings 1 +

Additional Findings 1 +

Glossary & General Resources

Summary of Findings

Reason for Testing

Other Key Clinical Findings

Primary Findings 1

Additional Findings 1

PRINT

Patient Information

Sample Information

Whole genome sequencing testing was ordered to identify a possible genetic cause for your symptoms. Your symptoms were reported to include: **Intellectual disability, Seizures with abnormal movements, Stereotypies**

None

MECP2

Clinical Diagnosis: A genetic cause for symptoms was found with a diagnosis of Rett syndrome.

Rationale: Variants in MECP2 have been identified in a number of neurodevelopmental disorders that mostly affect girls. These include classic Rett syndrome, atypical Rett syndrome which includes types with preserved expressive language, and milder forms of intellectual disability and autism. MECP2 mutations are usually lethal in boys, however there are reports of boys with MECP2 variants with severe neonatal encephalopathy usually resulting in death in early childhood. Girls with classic Rett syndrome have 6 to 18 months of apparently normal development before developing severe problems with language and communication, learning, coordination, and other brain functions. Early in childhood, affected girls lose purposeful use of their hands and begin making repeated hand wringing, washing, or clapping motions. They tend to grow more slowly than other children and have a small head size (microcephaly). Other signs and symptoms that can develop include breathing abnormalities, seizures, an abnormal side-to-side curvature of the spine (scoliosis), and sleep disturbances. In most cases mutations are de novo although rare cases of multiple affected family members have been reported.

Pertinent positives:

- Intellectual disability
- Seizures with abnormal movements
- Stereotypies

Pertinent negatives:

Mode of inheritance: de novo

Variants found:

- NM_001110792: c.952C>T; R318C; p.318R>C Monoallelic missense

BRCA2

Rationale: Adults with HBOC syndrome are at a higher risk to develop breast, ovarian and other cancer than people in the general population. Childhood cancers are NOT known to be associated with HBOC. Some families with HBOC syndrome also have a higher risk for certain other cancers, such as melanoma or pancreatic cancer. While it is possible to have HBOC and never develop cancer, it is important for anyone who has HBOC follow specific early cancer screening and prevention guidelines.

Mode of inheritance: Test Autosomal Dominant

Variants found:

- NM_000059: c.2T>G; M1R: p.1Mb>R Monoallelic missense

Confirmatory testing: Whole genome sequencing findings have been confirmed using a standard sequencing method

Sequencing Labs:

Personalis, Inc., Suite 202, 1350 Willow Road, Menlo Park, CA 94025, Phone: (650) 752-1349, Fax: (650) 752-1350

Interpretation Facility:

Genomic Medicine Institute, Geisinger Health System, 100 North Academy Ave, Danville, PA 17822-2620, (570) 214-7941