



MetaCore essentials

Indiana University November 2022

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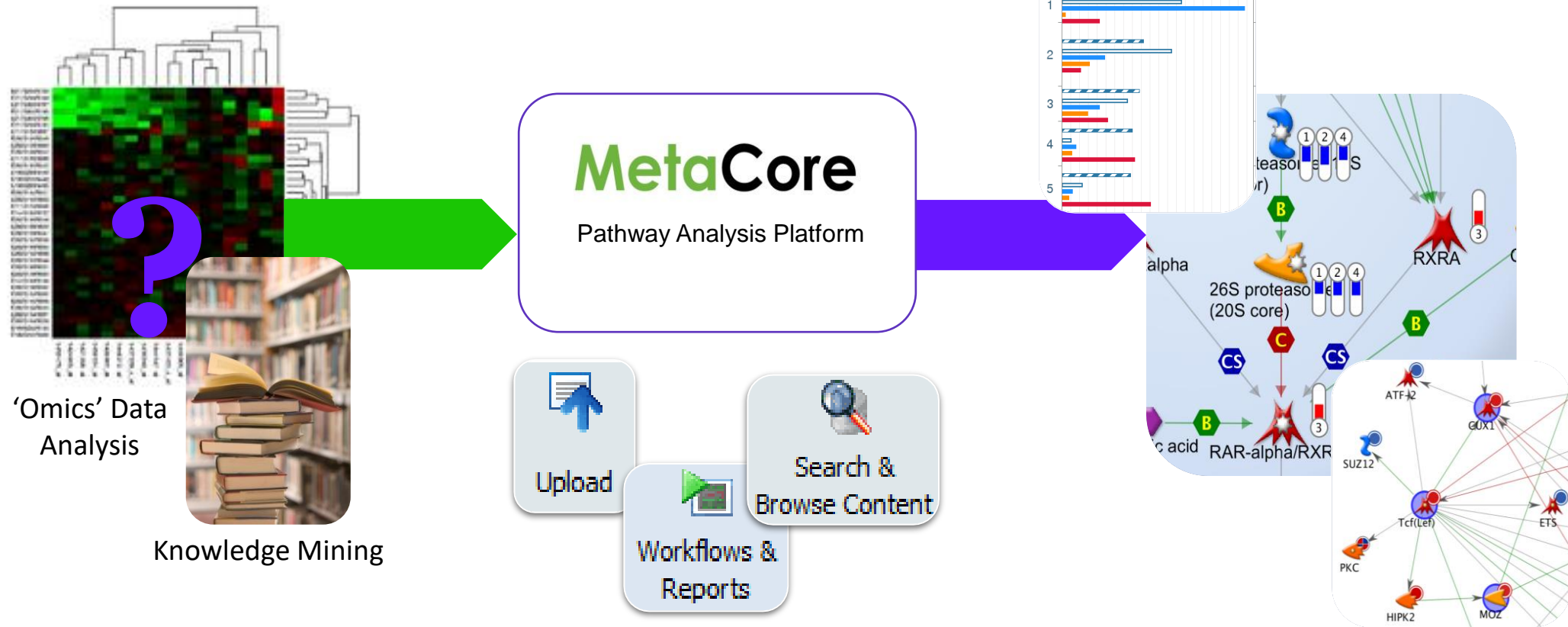
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Agenda

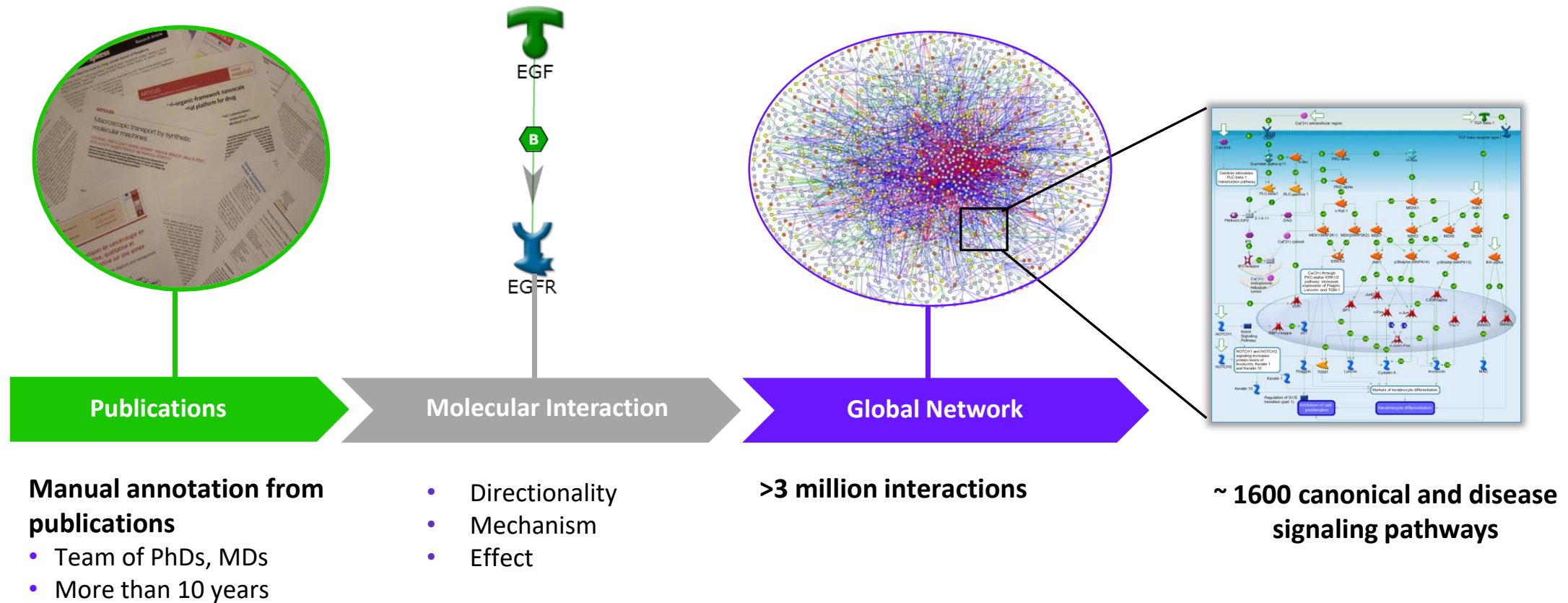
1. Overview of MetaCore
2. Live demo:
 - Using MetaCore as a knowledge mining tool
 - Uploading your data
 - Running a pathway map enrichment analysis
 - Building networks
3. Q&A

What is MetaCore?



- ✓ Knowledge mining
- ✓ Analyze and understand experimental findings (Omics data) in the context of validated biological pathways
- ✓ Generate and confirm hypotheses for novel biomarkers, targets, mechanisms of action

What is the content creation process?

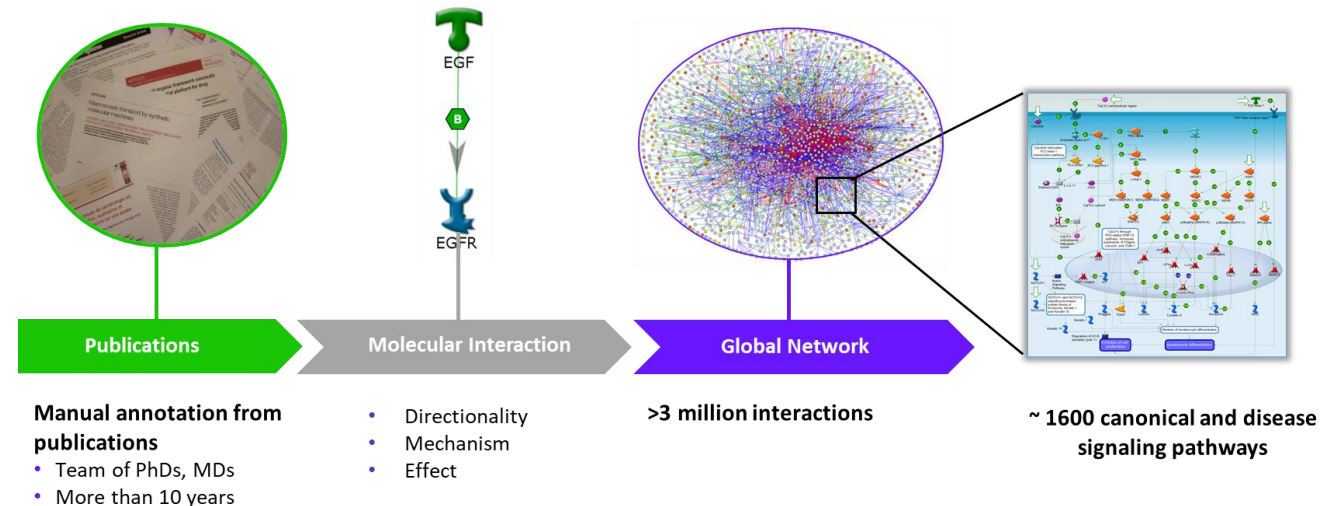


MetaCore Content

MetaCore	number
Human genes in network	29987
Mouse genes in network	28529
Rat genes in network	18675
Chemical compounds	565960
Drugs	4953
Endogenous compounds	3549
Metabolic reactions	51762
Transport reactions	4883
Processing Reactions	4490
Pubmed journals	3769
Pubmed records	3927194
Pubmed articles (unique)	326041
Total amount of interactions	3470443
- Protein – Protein	1545093
- Compound – Protein	1056791
- Compound – Compound	12564
- Metabolic enzyme -Reaction	62884
- Transporter – Reaction	5461
- Substrate, Product – Reaction	138484
- RNA – Protein	649166
Pathway maps	1593
- Human genes in maps	8218
- Mouse genes in maps	7498
- Rat genes in maps	7301
- Interactions in maps	36370

Differentiators compared to other solutions

- ✓ 100% manual curation by team of PhD- and MD-level research professionals
- ✓ Each molecular interaction is noted with mechanism, directionality & effect
- ✓ Unrestricted size and integration of different data types when building networks
- ✓ Comprehensive source of all critical data, including gene variant information, in one platform



Training data set

GSE95153 - Combining BET and MEK inhibitors synergistically targets NRAS mutant Melanoma cells

- Platform :Illumina NextSeq 500 (Homo sapiens)
- Comparison: BET inhibitor (JQ)
 MEK inhibitor (PD)
 BET / MEK combination

PMID: 29650805 “Co-targeting BET and MEK as salvage therapy for MAPK and checkpoint inhibitor-resistant melanoma”

Questions?

1. Visualize the impact of the 3 treatments in the expression of melanoma cells
2. Understand the impact of MEK inhibition in melanoma signaling pathways




MetaCore Login Page


<https://portal.genego.com/>

MetaCore


A Cortellis solution



[Home](#) [Support](#) [Training](#) [About Us](#)



Make target identification failure a thing of the past

[Learn more](#)


"Something that I do with MetaCore in one afternoon now, would have taken a week before."

Dr. Charles Lecellier
Principal Investigator
IGMM

Your GPS in Pathway Analysis

Whether you want to reduce the risk in your OMICs analysis, realize the potential of your biomarkers, or establish a target's mechanism of action, Clarivate Analytics has the right solution for you.

MetaCore

High quality biological systems content in context, giving you essential data and analytical tools to accelerate your scientific research.

MetaMiner Partnerships

A series of industry-academy partnerships on systems biology of common human diseases and stem cells, led by Clarivate Analytics.

MetaDrug

A leading systems pharmacology solution that incorporates extensive manually curated information on biological effects of small molecule compounds.

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.....

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1. Knowledge mining

EZ search for information related to melanoma

melanoma

Search

Advanced Search

Genomic Analysis

Most Popular Questions

Upload

Workflows & Reports

One-click Analysis

Build Network

Custom Content

Predict Compound Activity (MetaDrug)

Search & Browse Content

EZ Search

Name

Search

☐ Exact match

Objects Found

Genes (247)

Gene Aberrations (7933)

Proteins (782)

RNA (1110)

Compounds (2)

Network Objects (120)

Interactions (92)

Diseases (10)

Drugs (203)

Small Molecule Drugs (140)

Biologics (63)

Potential Disease Biomarkers (3234)

GO Processes (4)

Selected Diseases

Results

Show tree with all diseases

☐ Disease Details

Melanoma

Mesh Reference: D018328

Synonyms: Malignant Melanoma, Malignant Melanomas, Melanoma

Melanoma, Uveal

Synonyms: MELANOMA, UVEAL, Melanoma, Uveal

Melanoma, Cutaneous Malignant

Synonyms: MELANOMA, CUTANEOUS MALIGNANT, Melanoma, C

Melanoma, Amelanotic

Mesh Reference: D018328

Synonyms: Amelanotic Melanoma, Amelanotic Melanomas, Mel

Melanoma, Experimental

Mesh Reference: D008546

Synonyms: B16 Melanoma, B16 Melanomas, Cloudman S91 Mel

Melanoma

Disease

Export

Build Network

☒ Include Subfolders

☐ Show low trust content

Table of Contents

Summary

Causal Associations (by Gene)

Causal Associations (Endogenous Compounds)

Drugs & Therapeutic Agents

Pathway Maps

Summary

Description

A malignant neoplasm derived from cells that are capable of forming melanin, which from a pigmented nevus or malignant lentigo. Melanomas frequently metastasize widely. (Textbook of Dermatology, 4th ed, p2445)

Entry Terms

Melanoma; Malignant Melanoma; Malignant Melanomas; Melanoma, Malignant; Mel

External Databases

Mesh


D008545

Disease Ontologies

Chow Disease Tree

Clarivate™

What can I learn about genes being aberrantly expressed in melanoma?



Melanoma

Disease | [Export](#) | [Build](#)

Table of Contents

- [Summary](#)
- [Causal Associations \(by Gene\)](#)
- [Causal Associations \(Endogenous Compounds\)](#)
- [Drugs & Therapeutic Agents](#)
- [Pathway Maps](#)

Causal Associations (by Gene)

highlight text... 0/0

Result pages: 1 2 3 ... 179 (Showing results 1 to 20 of 3566)

#	Gene	Alteration Level	Alteration Type	Alteration Subtype	Details	Abundance	Activity/Gain/Loss of Function	Normal/Pathology Concentration	Subcellular Localization Change	Organ/Tissue Distribution	Disease	Info
1	GC	DNA level	Haplotype/SNP		GC HUMAN rs1155563(G)					Blood	Melanoma, Cutaneous Malignant	
2	MGMT	DNA level	Haplotype/SNP		MGMT HUMAN rs12917(T)					Melanocytes, Blood	Melanoma, Cutaneous Malignant	
3	TP53	DNA level	Haplotype/SNP		TP53 HUMAN c.807C>T(T)					Mucous Membrane	Melanoma	
4	CTNNBIP1	DNA level	Haplotype/SNP		CTNNBIP1 HUMAN c.1A>G(G)					Blood	Melanoma	
5	KLC3 , ERCC2	DNA level	Haplotype/SNP		ERCC2 HUMAN rs13181(C)_rs1799793(A)					Blood, Mouth Mucosa	Melanoma, Cutaneous Malignant	
6	GNAQ	DNA level	Haplotype/SNP		GNAQ HUMAN c.625C>T(T)					Uvea	Melanoma, Uveal	
7	ANKRD11 , LOC100287036	DNA level	Haplotype/SNP		ANKRD11 HUMAN rs2353033(A)					Blood	Melanoma	
8	CDKN2A	DNA level	Haplotype/SNP		CDKN2A HUMAN c.451C>T(T)					Melanocytes	Melanoma	
			Large Deletion		ACTA2 HUMAN Deletion / ACTA2 HUMAN Deletion					Melanocytes	Melanoma	
			STR/VNRT		IGF1 HUMAN c.?(CA)19		down					
					TP53 HUMAN c.860A>G(G)							
					BPIFA3 HUMAN rs17305657(T)							

Filter

- Alteration Level
- Alteration Type
- Alteration Subtype
- Abundance
- Activity/Gain/Loss of Function
- Subcellular Localization Change
- Organ/Tissue Distribution
- Disease
- Drug Targets/Biomarkers

Apply


References

Melanoma, Cutaneous Malignant

- ☒ Schäfer A, Emmert S, Kruppa J, Schubert S, Tzvetkov M, Mössner R, Reich K, Berking C. [No association of vitamin D metabolism-related polymorphisms and melanoma risk as well](#). Archives of dermatological research 2012 Jul;304(5):353-61. PMID: [22576141](#)

Experiment Details

Description	In a hospital-based case-control study including 30 (rs1155563, rs7041), and VDR (rs757343, rs73123) involved in the vitamin D metabolism was found to covariables.
Pathology name in article	Cutaneous melanoma



2. Uploading data

Upload data into MetaCore

1

Genomic Analysis

Most Popular Questions

Upload

Workflows & Reports

One-click Analysis

Build

You can upload your experimental data as well as list of genes/proteins/metabolites.

Upload Experiments with Gene or Protein IDs

Upload Metabolites

Upload Interactions

Upload Structures

Upload Genomic Variants

2

Data Analysis Wizard (General parser)

Step 1

Click "browse" to select file(s) to upload:

C:\Users\u6048039\Desktop\MelanomaData Browse...

Data format

Warning: do not mix IDs in the same co

Excel or plain text with tab separated fiel

Warning: Currently, Excel 2007 files are

tab separated fields or an older Excel ver

The file has to be in the following format:

Gene id *
[name 1]
...
[name n]

1	Gene	JQ/D fold	JQ/D p-value
2	ENSG00000017	-11.899845	2.83E-17
3	ENSG00000017	-3.7946079	2.29E-06
4	ENSG00000018	-5.7367193	1.00E-13
5	ENSG00000017	-9.7823006	1.29E-16
6	ENSG00000016	-11.417683	8.76E-27
7	ENSG00000012	-10.013915	1.09E-15
8	ENSG00000018	-14.591188	5.48E-31
9	ENSG00000010	-11.34163	1.66E-29

Next >>

3

Data Analysis Wizard (General parser)

Step 2

Only first 10 lines of your file are shown. Use horizontal scrolling if needed.

Use checkboxes against each row to specify table header lines

Specify the column types in your file:

File data

Experiments name prefix MelanomaDataset

Type	ENSEMBL IDs	Fold-change	P-value	Fold-change	P-value	Intensity
Name	Gene	JQ/D fold	JQ/D p-value	PD/D fold	PD/D p-value	Combo/D fold
<input checked="" type="checkbox"/>	Gene	JQ/D fold	JQ/D p-value	PD/D fold	PD/D p-value	Combo/D fold
<input type="checkbox"/>	ENSG000000175063	-11.89984457	2.82846E-17	-6.696517564	7.24527E-11	-360.0277313
<input type="checkbox"/>	ENSG000000171848	-3.794607942	2.29196E-06	-9.029358021	7.8051E-15	-233.3470959
<input type="checkbox"/>	ENSG000000189057	-5.736719315	1.00479E-13	-8.069565997	1.06915E-18	-187.2615365
<input type="checkbox"/>	ENSG000000178999	-9.782300588	1.28614E-16	-8.06897979	3.27817E-14	-215.2940858
<input type="checkbox"/>	ENSG000000168078	-11.41768256	8.76286E-27	-7.326696304	2.21615E-19	-230.814527
<input type="checkbox"/>	ENSG000000126787	-10.01391474	1.08513E-15	-7.09657905	4.68533E-12	-184.0147553
<input type="checkbox"/>	ENSG000000186185	-14.59118824	5.48202E-31	-8.357466807	2.4119E-21	-259.8326276

<< Back

Next >>

4

Data Analysis Wizard (General parser)

Step 3

Species

Choose species

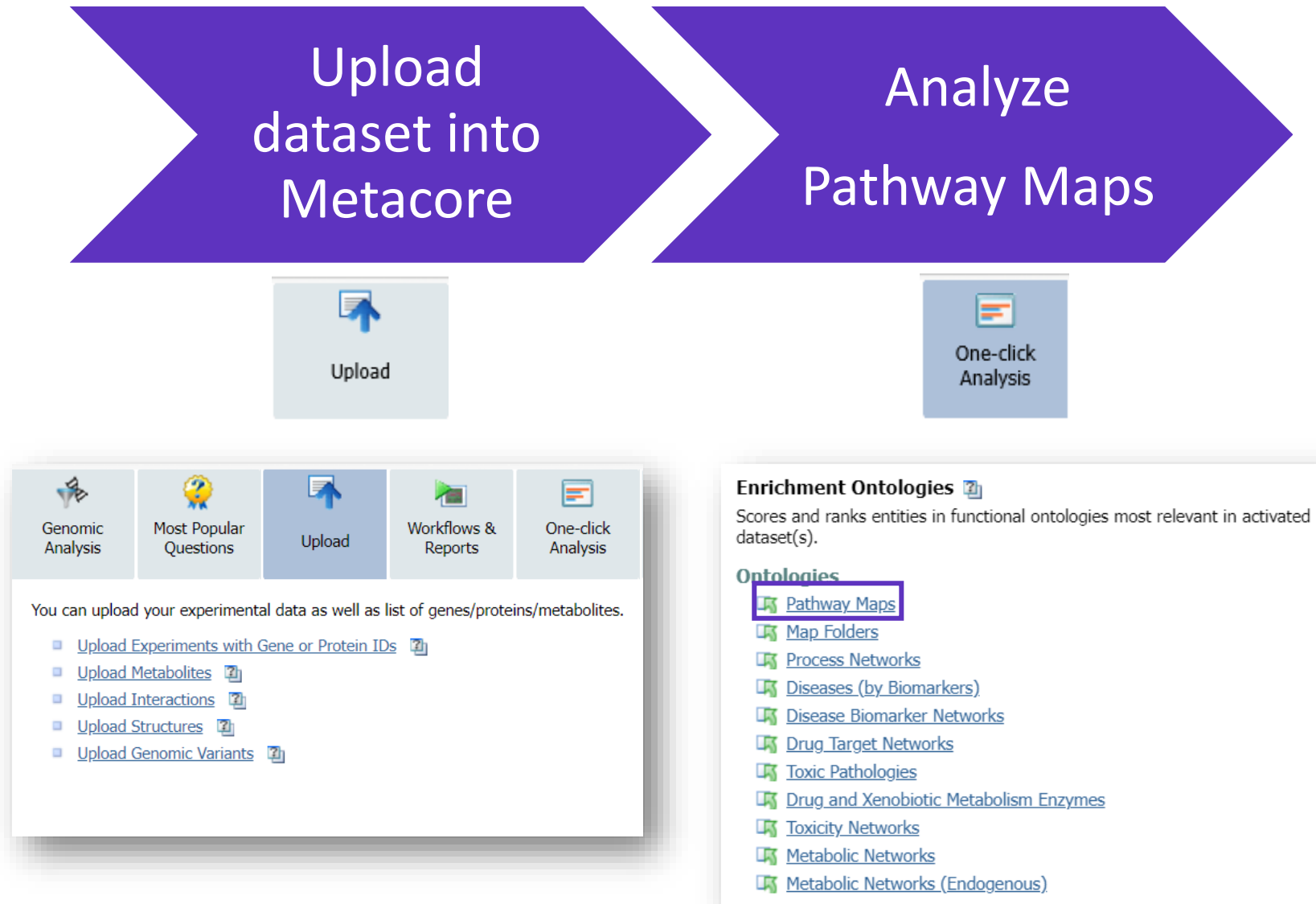
Homo sapiens

<< Back

Next >>

3. Pathway map enrichment

Which pathway maps are significantly enriched?

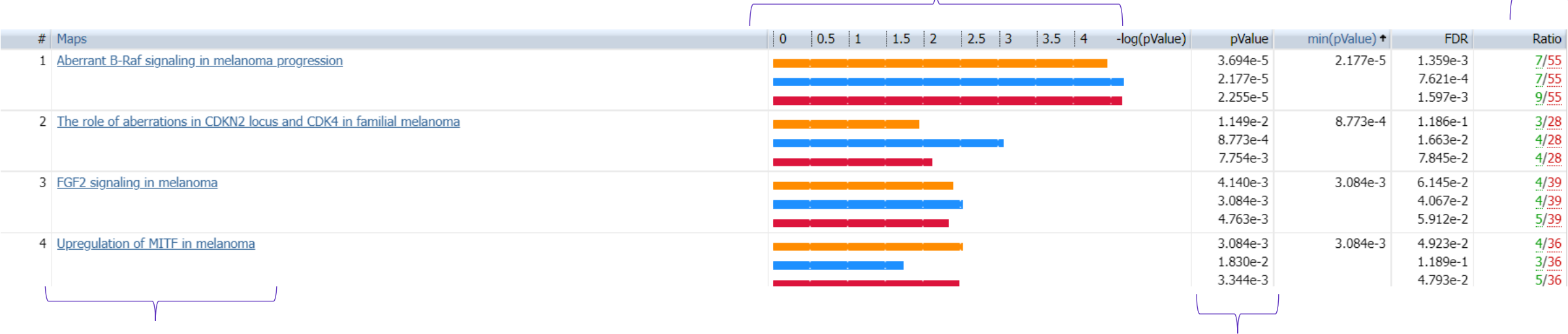


What overall process is impacted when comparing single treatment vs. combo treatment?

▼ Experiments			
<input checked="" type="checkbox"/>	Experiment name	Species	Network Objects
<input checked="" type="checkbox"/>	MelanomaDataset2_BETfold-change	Homo sapiens	474
<input checked="" type="checkbox"/>	MelanomaDataset2_MEKfold-change	Homo sapiens	398
<input checked="" type="checkbox"/>	MelanomaDataset2_Combo fold-change	Homo sapiens	858

Ratio of differentially expressed genes from dataset (GREEN) over all network objects in folder (RED)

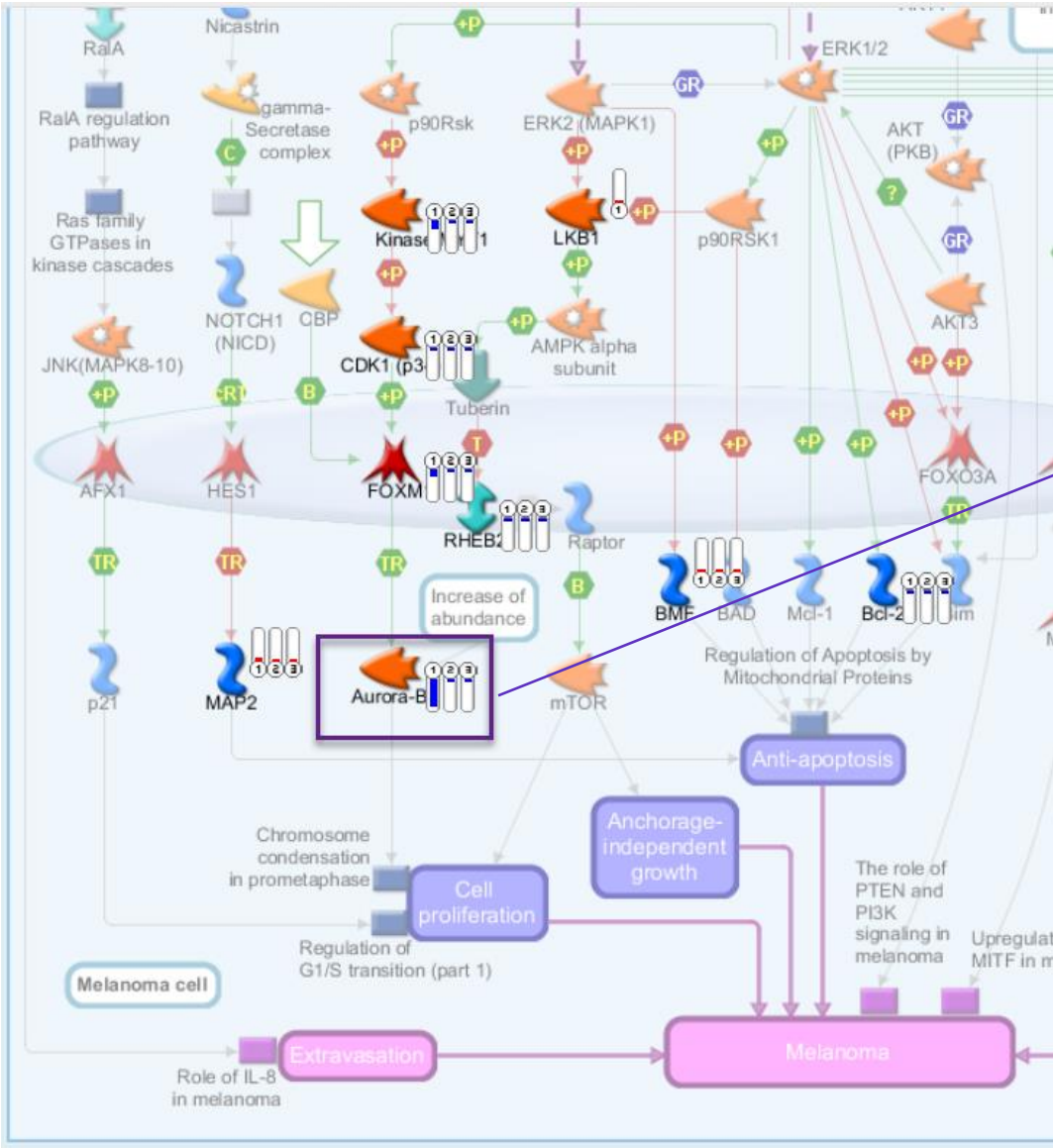
Graphical representation of $-\log(\text{pValue})$



Map folder name

Significance of overlap of differentially expressed genes in the folder

What pathways are disrupted by the differentially expressed genes?



Experimental Data close

Aurora-B

General Experiments Genomic Variant Experiments

By Objects

- [AURKB\(ENSG00000178999\)](#)

By Experiments

- (1) MelanomaDataset-New_Combo/D fold
- (2) MelanomaDataset-New_PD/D fold
- (3) MelanomaDataset-New_IQ/D fold

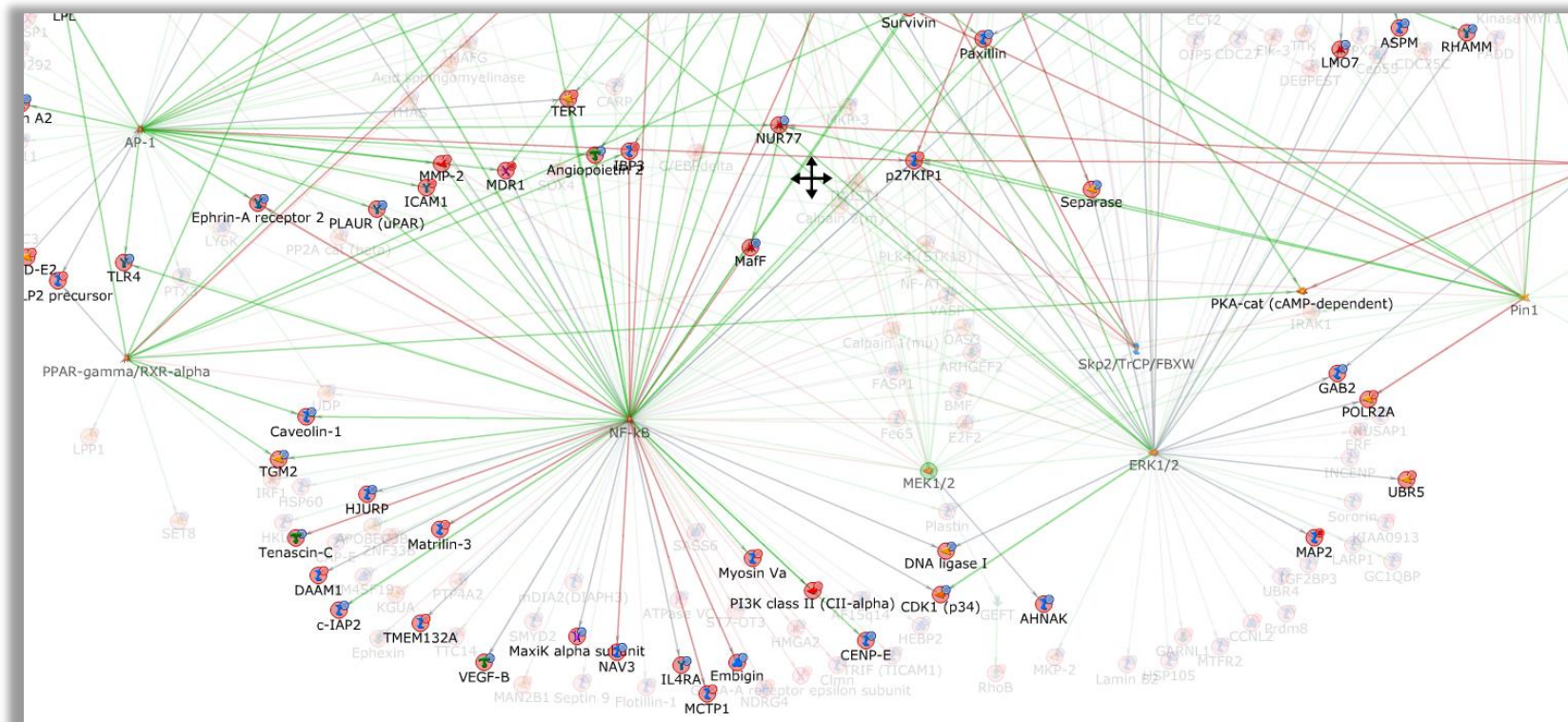
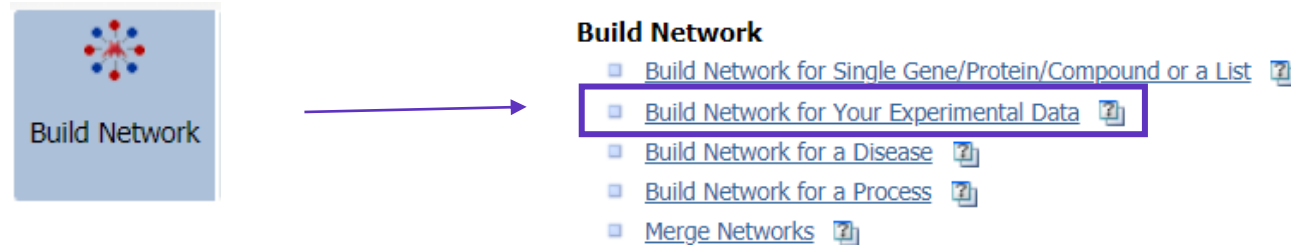
Objects

AURKB(ENSG00000178999)		
1	1: (1) MelanomaDataset-New_Co...	-215.29 [4.5e-68]
2	2: (2) MelanomaDataset-New_PD/...	-8.07 [3.3e-14]
3	3: (3) MelanomaDataset-New_IQ/...	-9.78 [1.3e-16]

Kinases such as Aurora-B are significantly down regulated in Combo/D treatment compared to BET/MEK inhibited single group in Melanoma progression pathway map

4. Building networks

Hypothesizing mechanisms of action behind MEK inhibitors by building network



Create a network from your experimental data

1

Home ▸ Active Data

Name	Type	Date
[...] Active Data		
Melanoma dataset GSE95153_PD/D FC_FF	GX	02/08/2019 15:05:31

2

File Edit View **Tools** Help

Workflows

Set Threshold and Background List...

Functional Ontology Enrichment

Interactome for Experiment(s)

Build Network from Active Data...

Build Network from the List...

Filter Experiments...

List Operations...

Home ▸ My Data

My Data

EXPERIMENTS

Eos_vs_neu

Eos_vs_neu

GENE LISTS

Eos_vs_neu

Eos_vs_neu

OR

2

Genomic Analysis Most Popular Questions Upload Workflows & Reports One-click Analysis **Build Network** Custom Content Predict Compound Activity (MetaDrug)

Build Network

[Build Network for Single Gene/Protein/Compound or a List](#)

[Build Network for Your Experimental Data](#)

[Build Network for a Disease](#)

[Build Network for a Process](#)

[Merge Networks](#)



Model Pathways

[Canonical Pathway Modeling](#)

Warning. This is a calculation intensive algorithm. Running time depends on the size of activated experiment(s). We strongly recommend to limit the size to 150 objects.

Create a network from your experimental data

There are 10 building algorithms with short description and recommendations

 Network options 

Choose building algorithm

Analyze network

Number of nodes in a network ⓘ 50

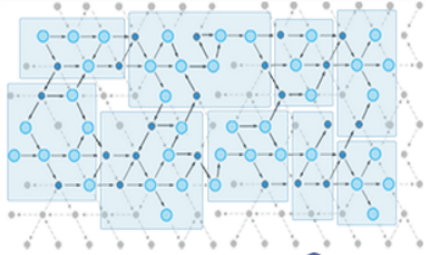
☒ Use canonical pathways (processing takes longer for large datasets)


Show additional options

Build network

Generates sub-networks enriched with seed nodes (nodes from root list = activated experiments). Sub-networks are ranked by a P-value and G-Score and interpreted in terms of Gene Ontology processes. ⓘ

We recommend 300-600 genes in input list for this algorithm. Analysis of larger datasets (>2,000 genes) is possible but calculation will take longer.

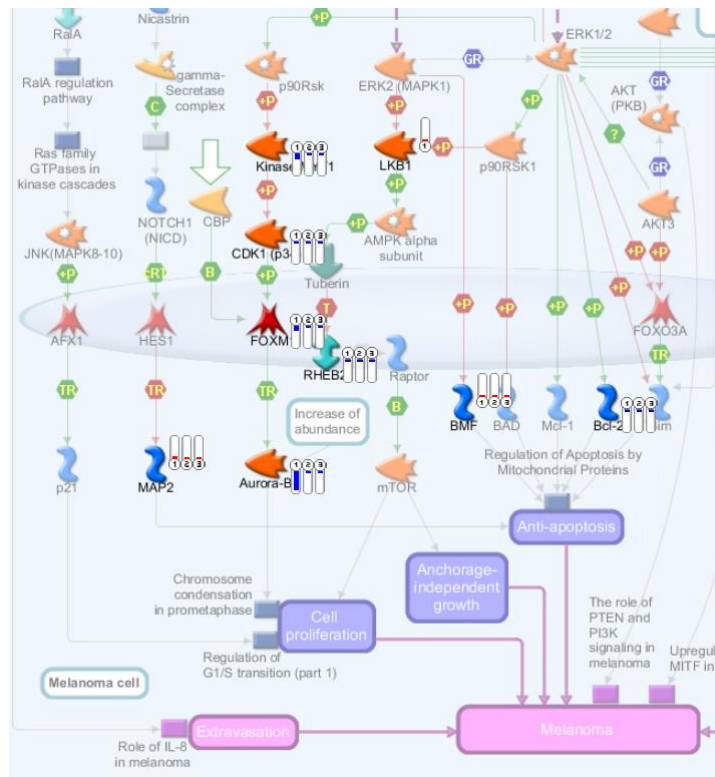


 Show legend

Use Additional Options (e.g. add molecular entity to the network) if necessary

Summary

- ✓ **Knowledge mining** – to better understand our disease/object of interest
- ✓ **Upload dataset** - to see what biological processes were significantly enriched in my data.
- ✓ **Pathway Maps**-look at pathway maps like “Aberrant B-Raf signaling in melanoma progression” to evaluate the overlay of my data.
- ✓ **Build Network** for PD/D (MEK inhibitor) hypothesizing its mechanisms of action.



Experiment name	Species	Network Objects
MelanomaDataset-New_JQ/D fold	Homo sapiens	879
MelanomaDataset-New_PD/D fold	Homo sapiens	767
MelanomaDataset-New_Combo/D fold	Homo sapiens	1189

More trainings this week!

MetaCore training webinar: Building networks tips & tricks – Tuesday November 15th 10am EST

In this webinar we will focus on the building network capability which allows you to quickly illustrate your findings. During the session we will discuss tips and tricks to optimally visualize and interpret your networks.

Using MetaCore™, a Cortellis™ solution, for multi-omics analysis - Wednesday November 16th 10am EST

During this session we will learn how to approach multi-omics analysis in MetaCore. Specifically, we will analyze metabolic, proteomic and gene expression data all at once to be able to hypothesize about their relationship.

We hope to see you there, bring your questions with you!



Questions?

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