

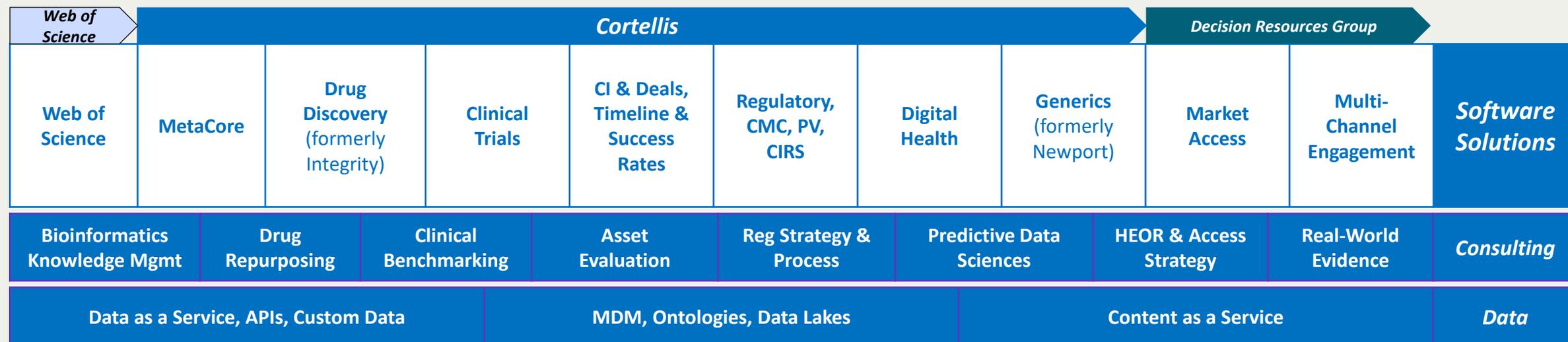
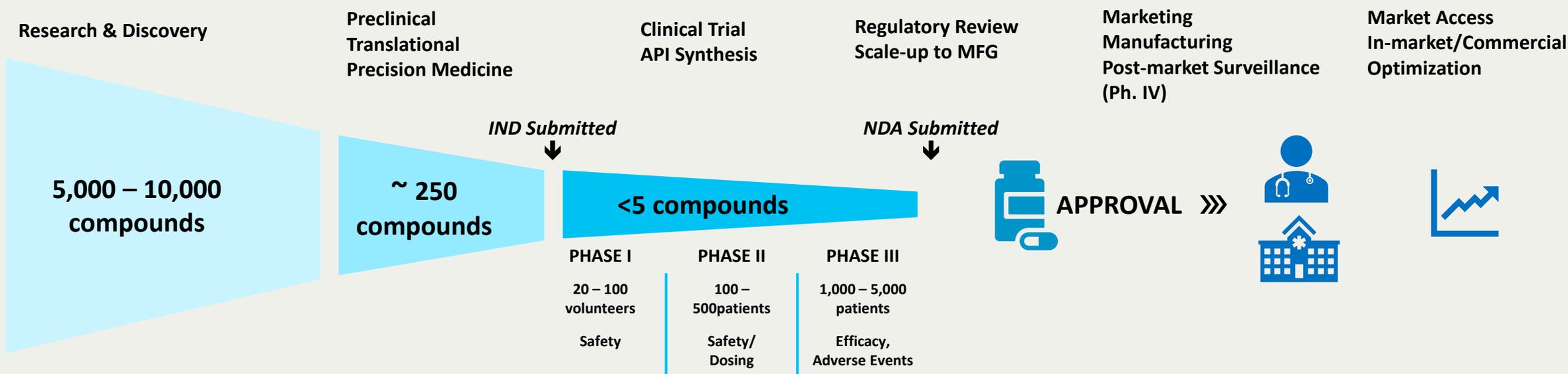
MetaCore

Accelerating the pace of innovation with trusted content, analytics, and technology

Kinsi Oberoi, Solution Scientist

04/06/2021

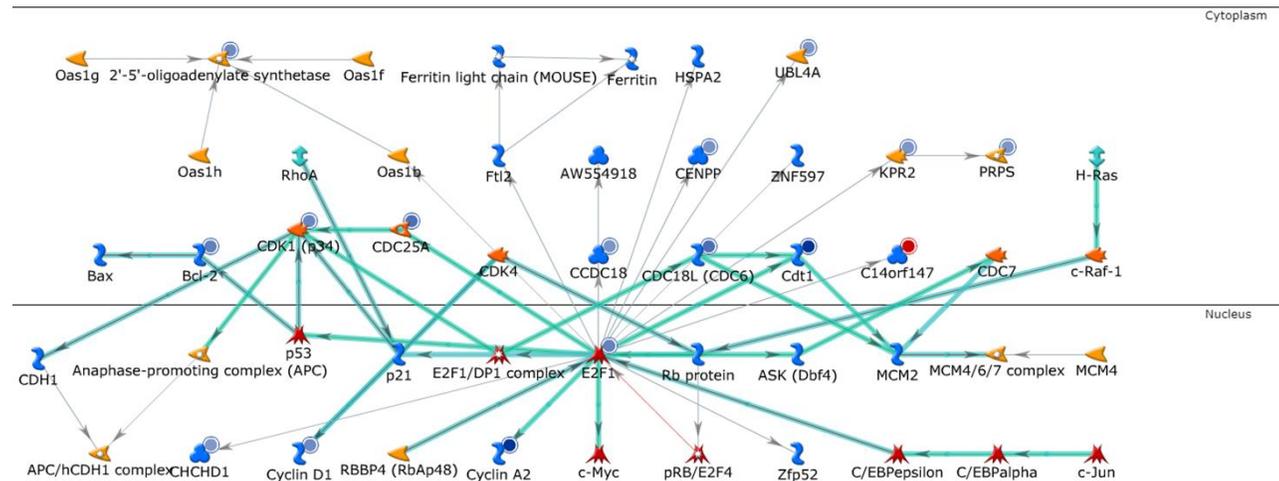
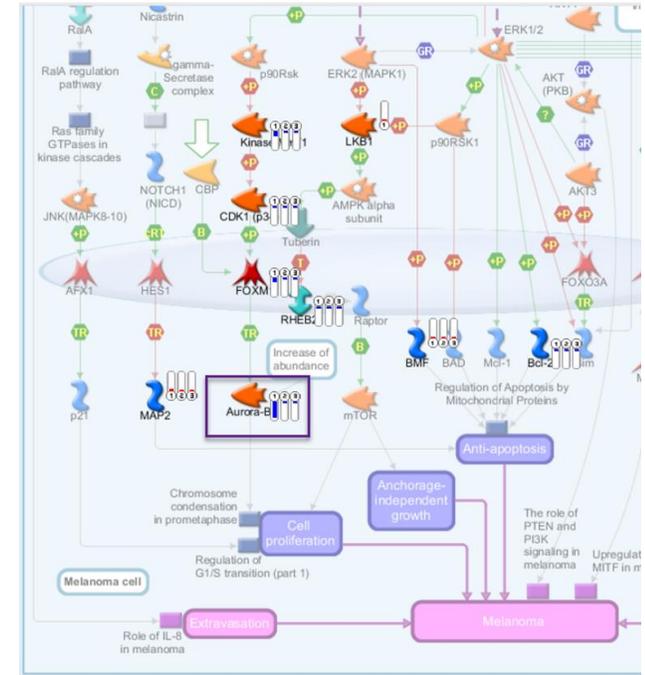
Our premier suite of solutions uniquely spans the entire innovation & product lifecycle



Agenda

Metacore Training

- Metacore Overview with live demo session showing how to:
 - Knowledge Mining
 - Upload data
 - Pathway Map Enrichment
 - Network Building
 - Metadrug
 - Q&A



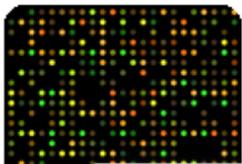
MetaCore: Your GPS in Pathway Analysis

INPUT

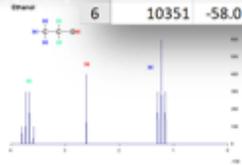
Data mining
Content Browsing



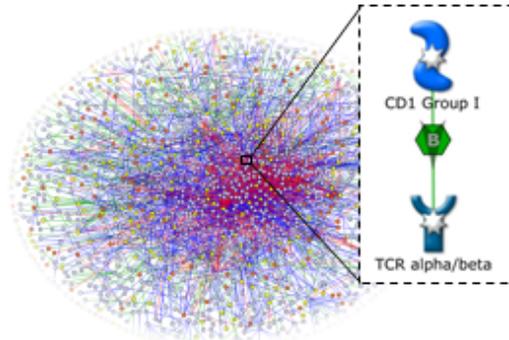
OMICs analysis



| | A | B | C |
|---|--------|-------------|----------|
| 1 | GeneID | Fold change | p-value |
| 2 | 25890 | -94.7858701 | 4.03E-07 |
| 3 | 7432 | -94.6483041 | 0.00016 |
| 4 | 91851 | -67.9404389 | 2.94E-06 |
| 5 | 1191 | -66.5434408 | 4.90E-07 |
| 6 | 10351 | -58.0187396 | 4.03E-07 |



METABASE



> 2,315,000 molecular interactions

From Human, mouse and rat

Manually curated by editorial team

(>50 PhD, MD)



3,701 journals

METACORE



1,567 Pathway Maps

- Understand your data in the context of validated biological pathways.
- Generate and confirm hypotheses for novel biomarkers, targets, mechanisms of action.

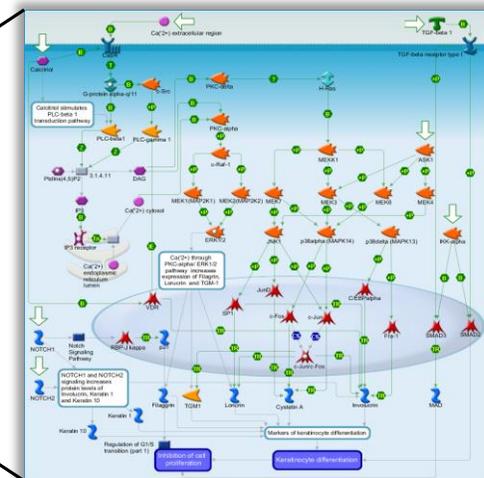
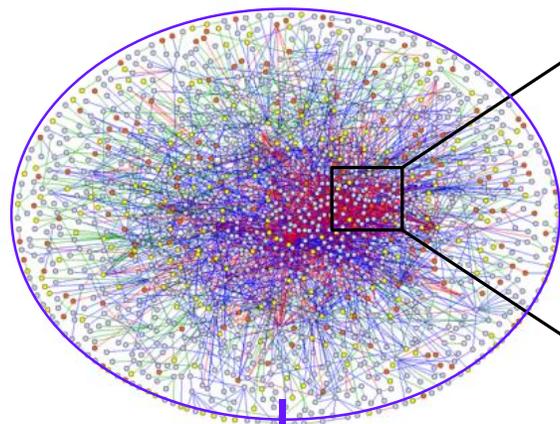
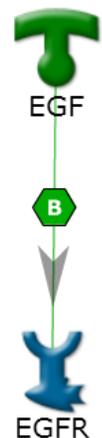
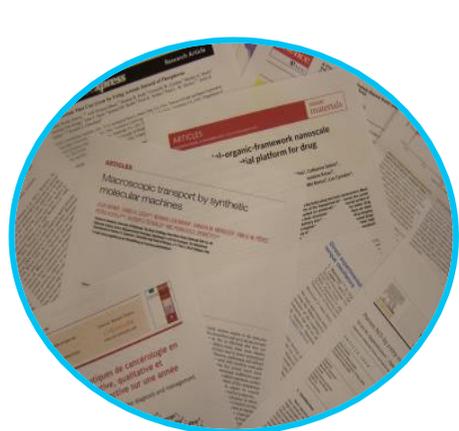
- Analyze molecular pathways and accelerate discovery research

MetaBase/ MetaCore Content Overview

| MetaBase | number |
|-----------------------------|--------|
| Human Genes | 61167 |
| Human SwissProt proteins | 20430 |
| Mouse genes | 72698 |
| Mouse SwissProt proteins | 17019 |
| Rat genes | 47891 |
| Rat SwissProt proteins | 8071 |
| Compounds | 891976 |
| Compounds with structure | 875221 |
| Endogenous compounds | 5448 |
| Nutritional compounds | 126 |
| Metabolites of xenobiotic | 32389 |
| Drugs | 9118 |
| - Biologics | 1362 |
| - Small Molecules | 7756 |
| - Approved drugs | 2290 |
| - Withdrawn drugs | 261 |
| - Clinical trial drugs | 4993 |
| - Discontinued drugs | 1187 |
| - Preclinical drugs | 251 |
| - Unknown | 136 |
| - Drug combination regimens | 8445 |

| MetaCore | number |
|---------------------------------|---------|
| Human genes in network | 25210 |
| Mouse genes in network | 22189 |
| Rat genes in network | 18780 |
| Chemical compounds | 435319 |
| Drugs | 4786 |
| Endogenous compounds | 3583 |
| Metabolic reactions | 40550 |
| Transport reactions | 3717 |
| Processing Reactions | 4410 |
| Pubmed journals | 3717 |
| Pubmed records | 2683859 |
| Pubmed articles (unique) | 294571 |
| Total amount of interactions | 2397073 |
| - Protein – Protein | 967668 |
| - Compound – Protein | 830890 |
| - Compound – Compound | 11699 |
| - Metabolic enzyme -Reaction | 51020 |
| - Transporter – Reaction | 4787 |
| - Substrate, Product – Reaction | 110739 |
| - RNA – Protein | 420278 |
| Pathway maps | 1578 |
| - Human genes in maps | 7750 |
| - Mouse genes in maps | 7042 |
| - Rat genes in maps | 6930 |
| - Interactions in maps | 33153 |

From Peer-Reviewed Publications to Signaling Pathways



Publications

Molecular Interaction

Global Network

207 publications cited for EGF-EGFR interaction

2,355,252 molecular interactions

1,545

CANONICAL AND DISEASE SIGNALING PATHWAYS

Manual annotation from 3,712 peer-reviewed journals (updated quarterly)

- 290,790 published articles cited with strong experimental evidence
- Team of PhDs & MDs curating for more than 10 years
- Every interaction has directionality, effect, mechanism, and source

Metacore Login Page

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

System Biology Solutions



Home Support Training About Us



Make target identification failure a thing of the past

Learn more



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.

LOGIN

Username

Password

Remember me

[Forgot your password?](#)

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

Dr. Charles Lecellier
Principal Investigator
IGMM

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Training Dataset

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

- Platform :Illumina NextSeq 500 (Homo sapiens)
- P value - 0.05, Threshold - 1
- Comparison: untreated
DMSO-treated
JQ1-treated (BET inhibitor)
PD901-treated (MEK inhibitor)
JQ1+PD901-combination treated

Question?



1.The impact of MEK inhibition of Signaling pathways in Melanoma?

2. Hypothesizing the relationship between the JQ/D and PD/D single treatments with the combo/D treatments?

Knowledge Mining

Do Ez search to find 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 A (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: D008546
Synonyms: Malignant Melanoma, Malignant Melanomas, Melanoma
- Melanoma, Uveal
Synonyms: MELANOMA, UVEAL, Melanoma, Uveal
- Melanoma, Cutaneous Malignant
Synonyms: MELANOMA, CUTANEOUS MALIGNANT, Melanoma, Cutaneous Malignant
- Melanoma, Amelanotic
Mesh Reference: D018328
Synonyms: Amelanotic Melanoma, Amelanotic Melanomas, Melanoma, Amelanotic
- Melanoma, Experimental
Mesh Reference: D008546
Synonyms: B16 Melanoma, B16 Melanomas, Cloudman S91 Melanoma, Experimental Melanoma

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; Melanoma, Experimental

External Databases

| | |
|------|---------|
| Mesh | D008546 |
|------|---------|

Disease Ontologies

Chow Disease Tree

What can I learn about genes being overly 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 ... 171 (Showing results 1 to 20 of 3419)

| # | 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 |
|----|---|------------------|---------------------|--------------------|---|-----------|--------------------------------|--------------------------------|---------------------------------|---------------------------|---|------|
| 11 | IGF1 | DNA level | Gene rearrangements | STR/VNTR | IGF1_HUMAN_c.1(CA)19 | | down | | | blood | Melanoma, Cutaneous Malignant | |
| 12 | TP53 | DNA level | Haplotype/SNP | | TP53_HUMAN_c.860A>G(G) | | | | | Melanocytes | Melanoma, Cutaneous Malignant | |
| 13 | BPIFA3 | DNA level | Haplotype/SNP | | BPIFA3_HUMAN_rs17305657(T) | | | | | Blood | Melanoma, Cutaneous Malignant | |
| 14 | TGFA | DNA level | Locus change | | TGFA_HUMAN_locus_change_2p13 | | | | | Melanocytes | Melanoma | |
| 15 | KIT | DNA level | Haplotype/SNP | | KIT_HUMAN_c.1673A>G(G) | | | | | Melanocytes, Skin | Melanoma | |
| 16 | MMP28 | DNA level | Haplotype/SNP | | MMP28_HUMAN_c.728G>C(C) | | | | | Melanocytes | Melanoma | |
| 17 | HLA-DRB3 , HLA-DRB1 | DNA level | Haplotype/SNP | | HLA-DRB1_HUMAN_DRB1*1103 | | | | | Leukocytes | Melanoma | |
| 18 | BRAF | DNA level | Haplotype/SNP | | BRAF_HUMAN_rs121913227(GT) / BRAF_HUMAN_rs121913227((A)2) | | | | | Melanocytes | Melanoma | |
| 19 | RASEF | DNA level | Epigenetics | Methylation | RASEF_HUMAN_Methylation | up | | | | Uvea | Melanoma, Uveal | |
| 20 | KIT | DNA level | Haplotype/SNP | | KIT_HUMAN_c.1672A>G(G) | | | | | Melanocytes | Melanoma | |

Upload 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 column. Excel or plain text with tab separated fields.

Warning: Currently, Excel 2007 files are not supported. The file has to be in the following format:

| Gene id * | JQ/D fold | JQ/D p-value |
|-----------|-----------|--------------|
| [name 1] | | |
| ... | | |
| [name n] | | |

| | | | |
|---|-----------------|------------|--------------|
| 1 | Gene | JQ/D fold | JQ/D p-value |
| 2 | ENSG00000175063 | -11.899845 | 2.83E-17 |
| 3 | ENSG00000171848 | -3.7946079 | 2.29E-06 |
| 4 | ENSG00000189057 | -5.7367193 | 1.00E-13 |
| 5 | ENSG00000178999 | -9.7823006 | 1.29E-16 |
| 6 | ENSG00000168078 | -11.417683 | 8.76E-27 |
| 7 | ENSG00000126787 | -10.013915 | 1.09E-15 |
| 8 | ENSG00000186185 | -14.591188 | 5.48E-31 |
| 9 | ENSG00000186185 | -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"/> | ENSG00000175063 | -11.8998457 | 2.82846E-17 | -6.696517564 | 7.24527E-11 | -360.0277313 |
| <input type="checkbox"/> | ENSG00000171848 | -3.794607942 | 2.29196E-06 | -9.029358021 | 7.8051E-15 | -233.3470959 |
| <input type="checkbox"/> | ENSG00000189057 | -5.736719315 | 1.00479E-13 | -8.069565997 | 1.06915E-18 | -187.2615365 |
| <input type="checkbox"/> | ENSG00000178999 | -9.782300588 | 1.28614E-16 | -8.06897979 | 3.27817E-14 | -215.2940858 |
| <input type="checkbox"/> | ENSG00000168078 | -11.41768256 | 8.76286E-27 | -7.326696304 | 2.21615E-19 | -230.814527 |
| <input type="checkbox"/> | ENSG00000126787 | -10.01391474 | 1.08513E-15 | -7.09657905 | 4.68533E-12 | -184.0147553 |
| <input type="checkbox"/> | ENSG00000186185 | -14.59118824 | 5.48202E-31 | -8.357466807 | 2.4119E-21 | -259.8326276 |

<< Back Next >>

4

Data Analysis Wizard (General parser)

Step 3

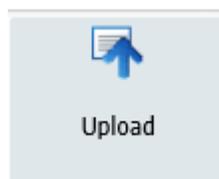
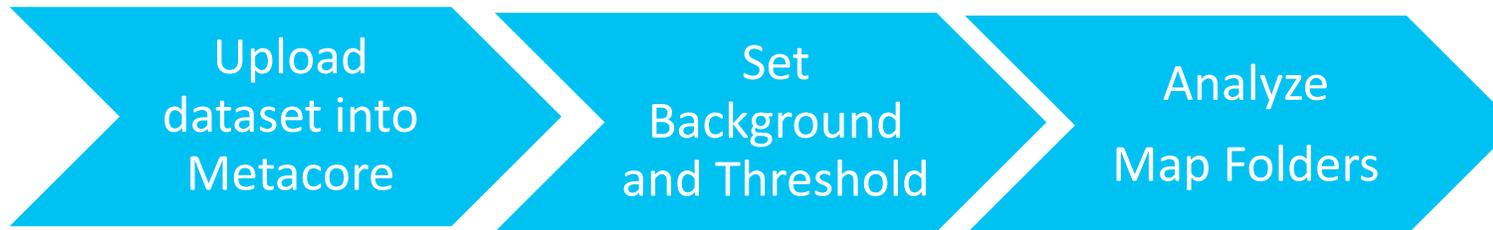
Species

Choose species: Homo sapiens

<< Back Next >>

Pathway Map Enrichment

Which maps are significantly enriched



Genomic Analysis | Most Popular Questions | **Upload** | Workflows & Reports | One-click Analysis

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

Background List and Threshold

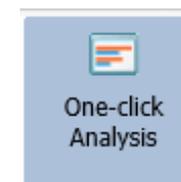
| | Threshold | P Threshold | |
|-----------|-----------|-------------|------------|
| General | 1 | 0.05 | Statistics |
| Metabolic | 0 | 1 | Statistics |

Background List

List Source: Array Gene list Network object list

List Name: Default

Cancel OK



Enrichment Ontologies

Scores and ranks entities in functional ontologies most relevant in activated dataset(s).

Ontologies

- Pathway Maps
- Map Folders**
- Process Networks
- Diseases (by Biomarkers)
- Disease Biomarker Networks
- Drug Target Networks
- Toxic Pathologies
- Drug and Xenobiotic Metabolism Enzymes
- Toxicity Networks
- Metabolic Networks
- Metabolic Networks (Endogenous)

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

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

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

| # | Map folders | 0 | 5 | 10 | 15 | 20 | 25 | $-\log(\text{pValue})$ | pValue | min(pValue) † | FDR | Ratio |
|---|-------------------------------|--------------|---|----|----|----|----|------------------------|-----------|---------------|----------|-------|
| 1 | Cell cycle and its regulation | [Orange bar] | | | | | | 1.291e-29 | 1.014e-33 | 8.648e-28 | 107/991 | |
| | | [Blue bar] | | | | | | 1.014e-33 | 6.792e-32 | 105/991 | | |
| | | [Red bar] | | | | | | 2.336e-28 | 1.565e-26 | 123/991 | | |
| 2 | Colorectal Neoplasms | [Orange bar] | | | | | | 8.797e-20 | 6.222e-27 | 1.965e-18 | 124/1660 | |
| | | [Blue bar] | | | | | | 3.864e-22 | 8.629e-21 | 118/1660 | | |
| | | [Red bar] | | | | | | 6.222e-27 | 2.084e-25 | 164/1660 | | |
| 3 | Lung cancer | [Orange bar] | | | | | | 1.661e-20 | 1.824e-26 | 5.565e-19 | 150/2213 | |
| | | [Blue bar] | | | | | | 3.838e-22 | 8.629e-21 | 140/2213 | | |
| | | [Red bar] | | | | | | 1.824e-26 | 4.074e-25 | 195/2213 | | |
| 4 | Melanoma | [Orange bar] | | | | | | 8.908e-17 | 4.263e-23 | 1.194e-15 | 119/1691 | |
| | | [Blue bar] | | | | | | 2.183e-17 | 2.089e-16 | 110/1691 | | |
| | | [Red bar] | | | | | | 4.263e-23 | 7.141e-22 | 158/1691 | | |

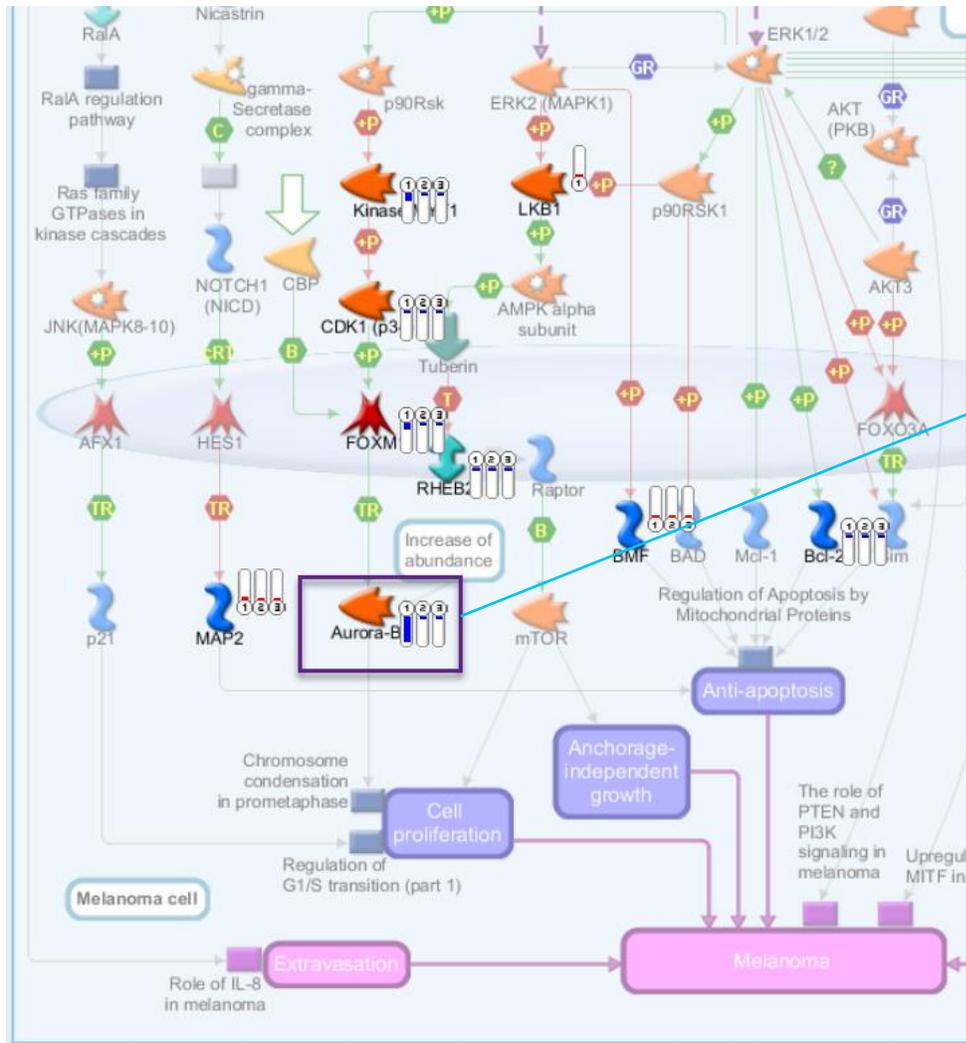
Map folder name

Significance of overlap of differentially expressed genes in the folder

Marked difference in the presence of differentially expressed genes between single treatment and combo treatment in Melanoma Map folder

What pathways are disrupted by the differentially expressed genes?

Aberrant B-Raf signaling in melanoma progression



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_JQ/D fold

Objects

| Object ID | Experiment | Value | Significance |
|-----------|--------------------------------|---------|--------------|
| 1 | (1) MelanomaDataset-New_Co... | -215.29 | [4.5e-68] |
| 2 | (2) MelanomaDataset-New_PD/... | -8.07 | [3.3e-14] |
| 3 | (3) MelanomaDataset-New_JQ/... | -9.78 | [1.3e-16] |

Kinase such as Aurora-B are significantly down regulated in Combo/D treatment compared to JQ /D and PD/D single group in Melanoma progression pathway map

Compare Experiment

Compare experiment workflow



Background List and Threshold

| | Threshold | P Threshold | |
|-----------|--------------------------------|-----------------------------------|---|
| General | <input type="text" value="1"/> | <input type="text" value="0.05"/> | <input type="button" value="Statistics"/> |
| Metabolic | <input type="text" value="0"/> | <input type="text" value="1"/> | <input type="button" value="Statistics"/> |

Background List

List Source: Array Gene list Network object list

List Name:

Data Analysis Workflows
A set of simple step-by-step wizards for analysis of your data.

- [Enrichment Analysis](#)
- [Analyze Single Experiment](#)
- [Compare Experiments](#)**
- [Compare Compounds](#)
- [Toxicity Analysis](#)
- [Biomarker Assessment](#)
- [Interactome Analysis](#)

Question:
What process is impacted when comparing patient groups?

What process is impacted when comparing patient groups ?

| Experiment name | Species | Network Objects |
|------------------------------|--------------|-----------------|
| MelanomaDataset_JQ/D fold | Homo sapiens | 889 |
| MelanomaDataset_PD/D fold | Homo sapiens | 777 |
| MelanomaDataset_Combo/D fold | Homo sapiens | 1200 |



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

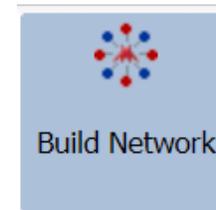
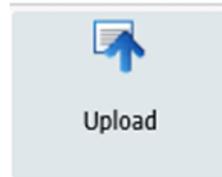
Graphical representation of $-\log(pValue)$

| # | Maps | $-\log(pValue)$ | pValue | pValue | FDR | Ratio |
|---|--|-----------------|--|----------|--|--------------------------------------|
| 1 | Aberrant B-Raf signaling in melanoma progression | | 1.000e+0 6.480e-5 1.000e+0 1.000e+0 3.480e-1 | 6.480e-5 | 1.000e+0 3.237e-3 1.000e+0 1.000e+0 4.223e-1 | 0/55 8/55 0/55 0/55 1/55 |
| 2 | Abnormalities in cell cycle in SCLC | | 1.937e-1 2.356e-8 1.000e+0 1.000e+0 2.095e-2 | 2.356e-8 | 3.722e-1 3.007e-6 1.000e+0 1.000e+0 2.374e-1 | 1/29 9/29 0/29 0/29 2/29 |
| 3 | Anti-apoptotic action of ErbB2 in breast cancer | | 1.000e+0 2.706e-4 2.706e-4 1.000e+0 | 2.706e-4 | 1.000e+0 8.404e-3 8.404e-3 1.000e+0 | 0/51 7/51 7/51 0/51 |

Map name

Significance of overlap of differentially expressed genes in the Map

Build Network for your Experimental Data



Genomic Analysis | Most Popular Questions | **Upload** | Workflows & Reports | One-click Analysis

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

Background List and Threshold

| | Threshold | P Threshold | |
|-----------|--------------------------------|-----------------------------------|---|
| General | <input type="text" value="1"/> | <input type="text" value="0.05"/> | <input type="button" value="Statistics"/> |
| Metabolic | <input type="text" value="0"/> | <input type="text" value="1"/> | <input type="button" value="Statistics"/> |

Background List

List Source: Array Gene list Network object list

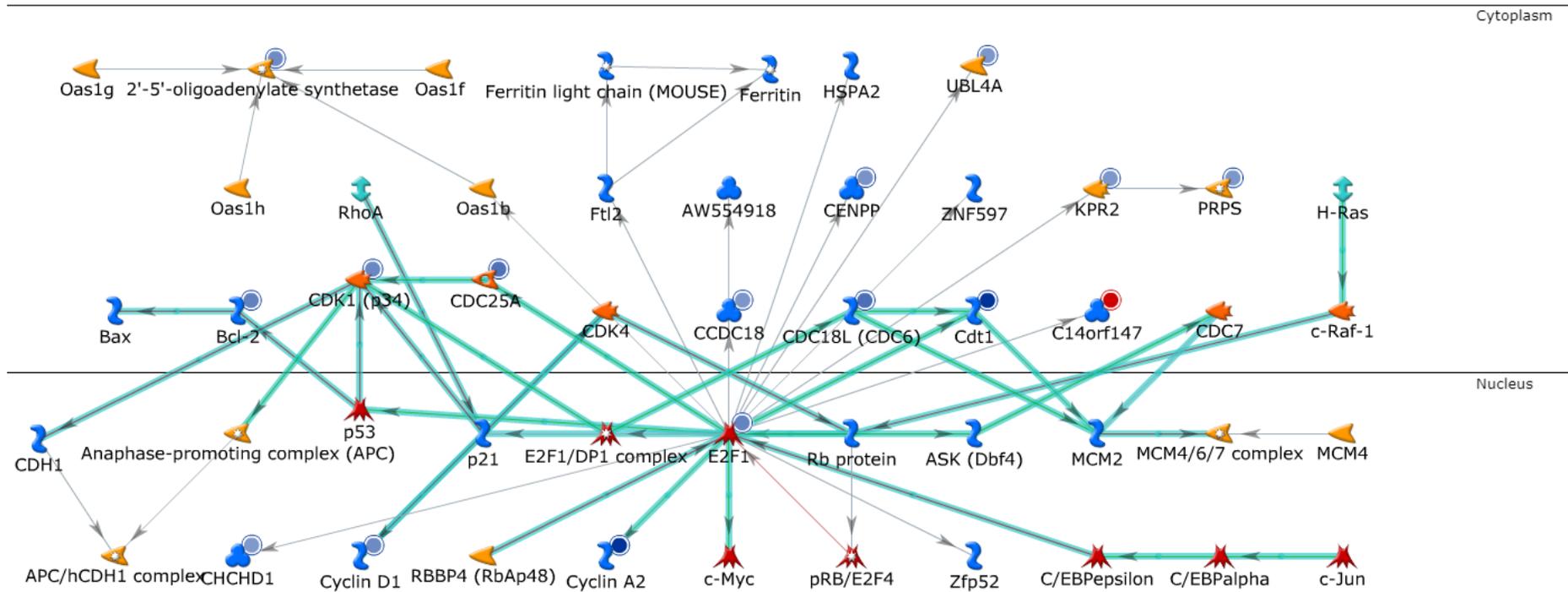
List Name:

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](#)

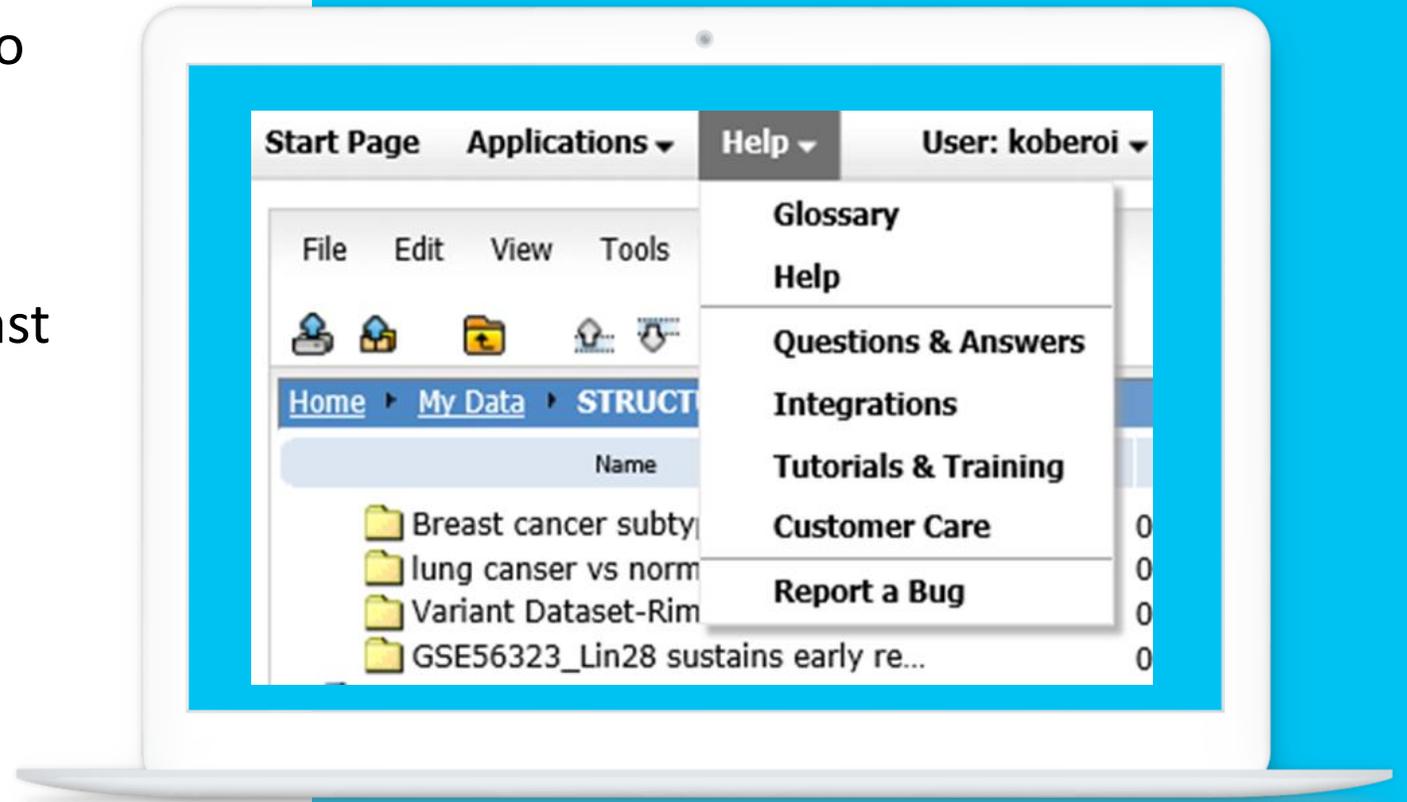
Network Building

Hypothesizing mechanisms of action behind MEK inhibitors by building network



Learn More

- You can learn more about upcoming webinars by going on to Help tab, Tutorials&Training, on MetaCore's start page
- Look for Pendo on left corner of landing page introduced earlier last month to help deliver a great product experience

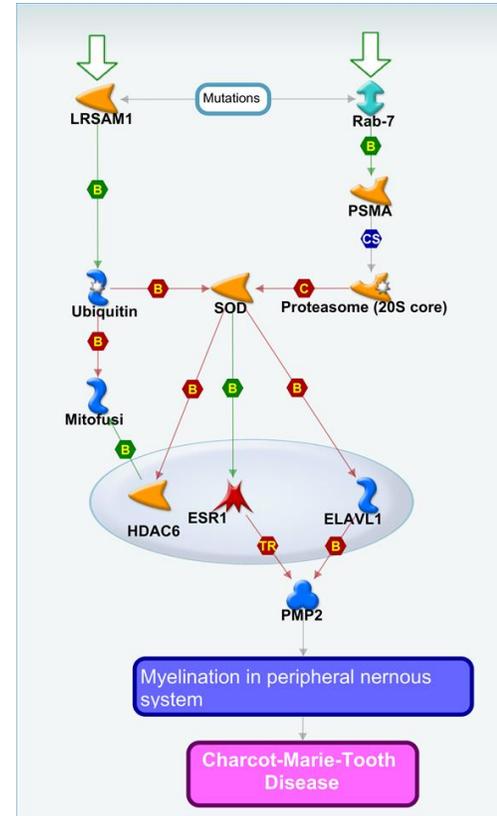


Screen caption

What would be covered in advanced training session

Pick topic for next session

1. Find Key Hubs using Over-Connectivity Analysis
2. Network building
3. Using Microarray repository for gene comparisons against public data
4. Constructing your own pathway maps
5. Analyzing multi-omics data (RNA-seq, proteomics, metabolomics, etc)



You've invited! MetaCore Advanced training

Training session details:

Please join us in this hands-on training session to learn further insights about the Clarivate MetaCore resource.

- Date: Tue April 13, 2021
- Time: 12pm – 1.30pm

[Sign up](#)

Based on your feedback during the first introductory MetaCore session on April 6th, we have designed a tailored training to cover your main areas of interest.

Come to this **hands-on Advanced session** to learn:

- How to work with multi-omics data.
- How to upload metabolite data.
- How to run enrichment analysis.

Don't forget to bring your questions with you!



Host:
Kinsi Oberoi
Solution Scientist
Clarivate



Thank you

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