MetaCore essentials

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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

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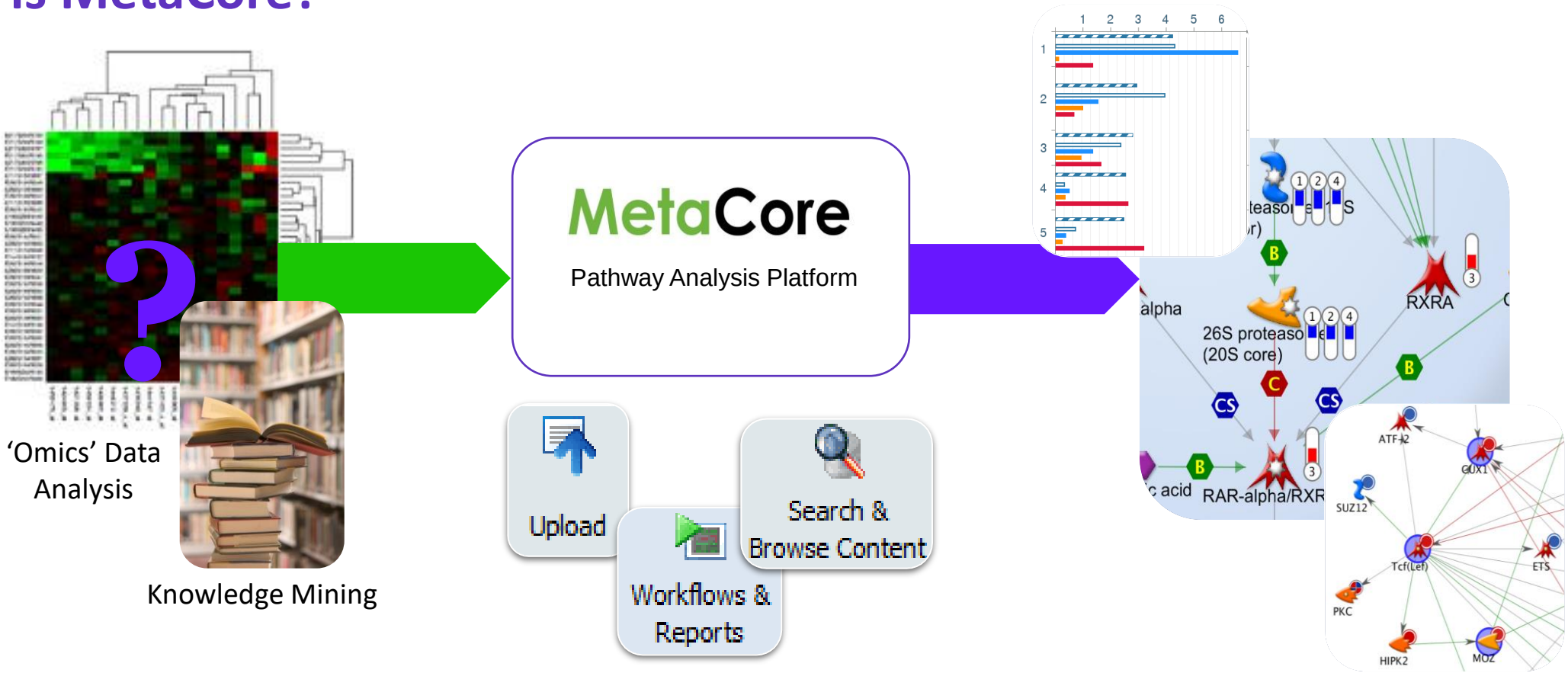
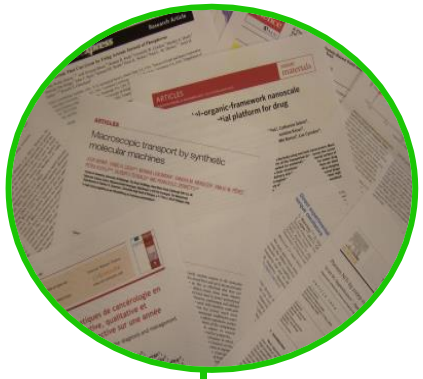
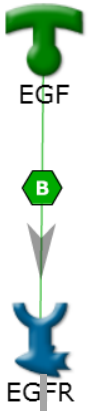
What is MetaCore?

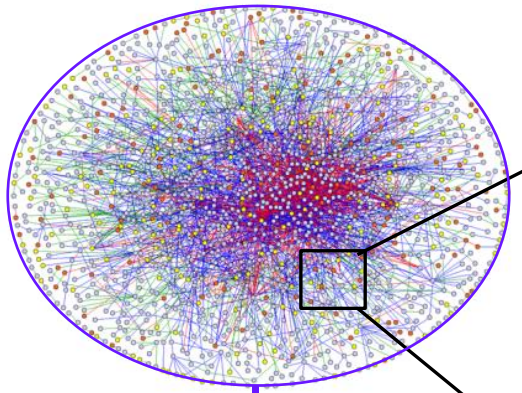


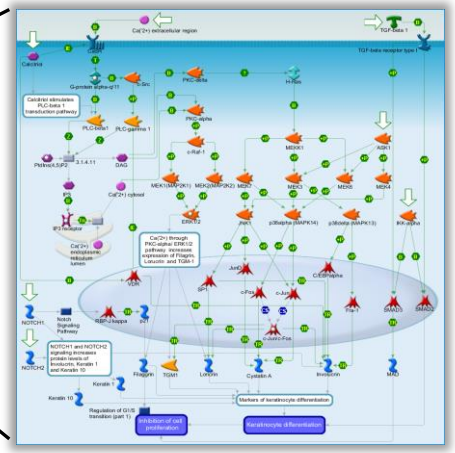
- ✓ Knowledge mining
- ✓ Analyze and understand experimental findings (Omics data) in the context of validated biological pathways
- ✓ Generate and confirm hypotheses for novel biomarkers, targets, mechanisms of action

What is the content creation process?









Publications

Manual annotation from publications

- Team of PhDs, MDs
- More than 10 years

Molecular Interaction

- Directionality
- Mechanism
- Effect

Global Network

>3 million interactions

~ 1600 canonical and disease signaling pathways

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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

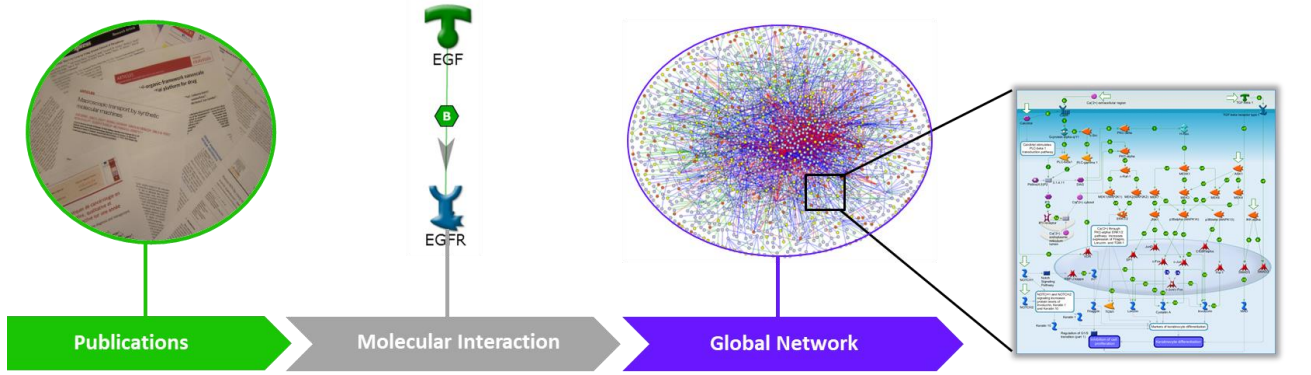
Differentiators compared to other solutions

✓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



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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

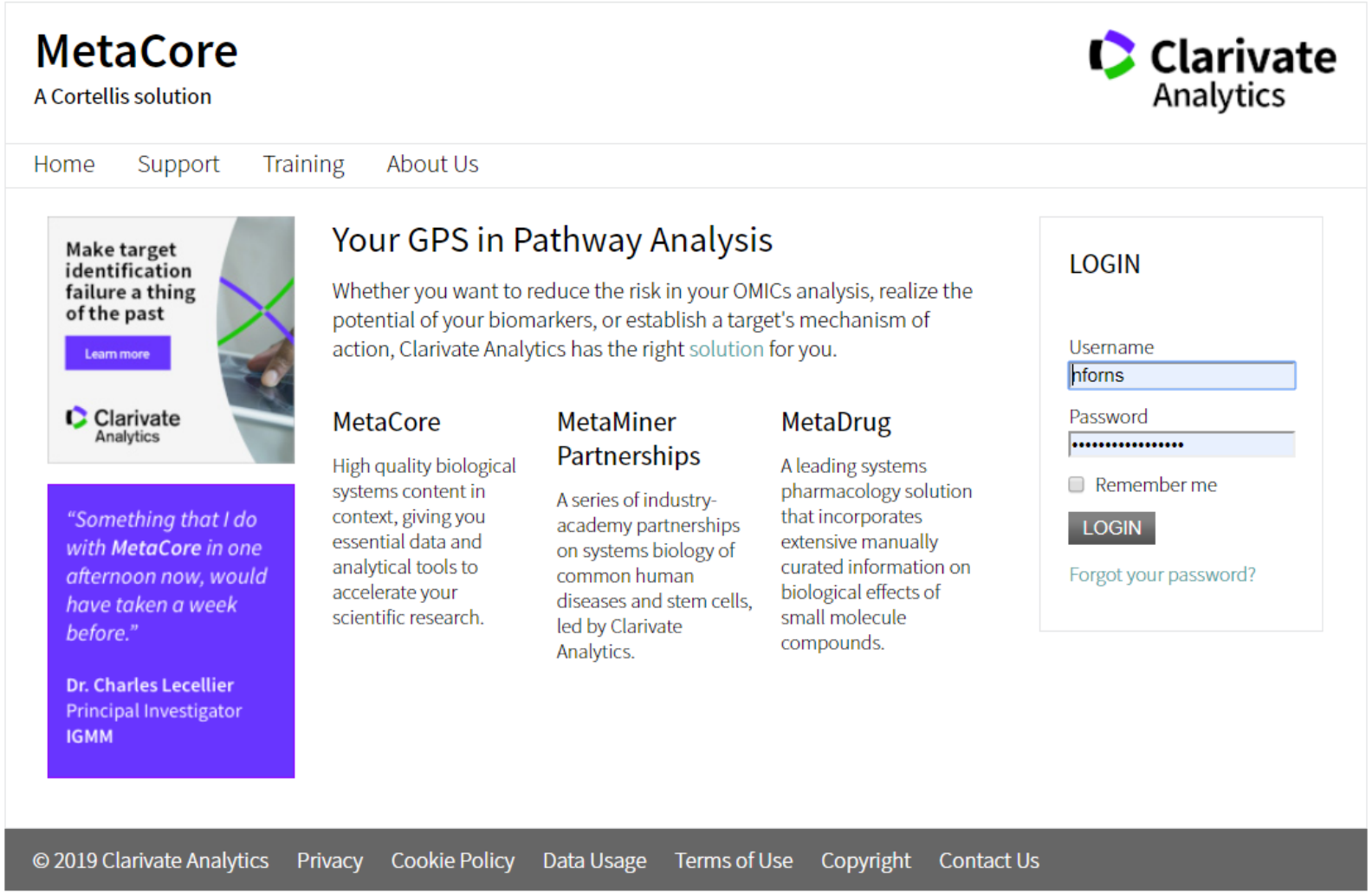
PMID: 29650805 “Co-targeting BET and MEK as salvage therapy for MAPK and checkpoint inhibitor-resistant melanoma”

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/



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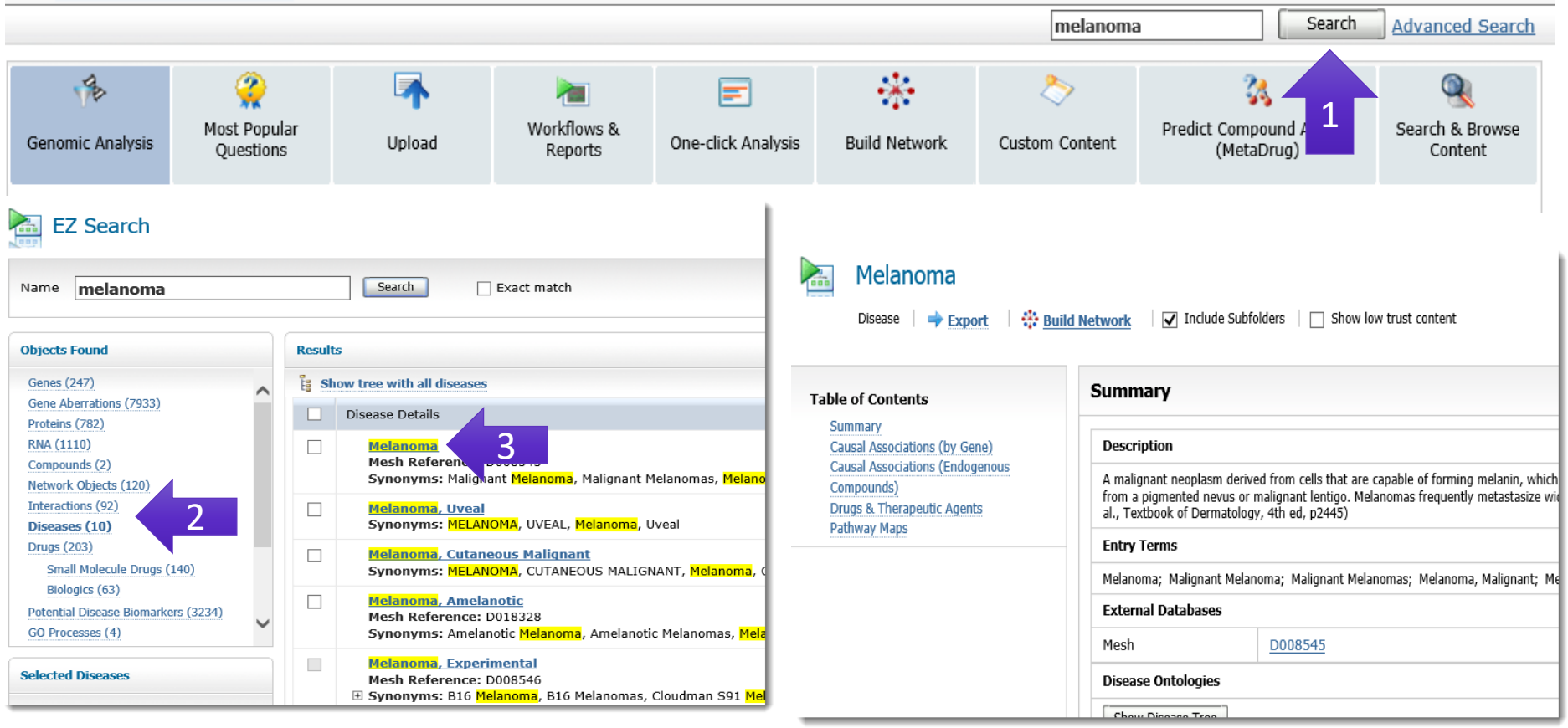
1. Knowledge mining

EZ search for information related to melanoma



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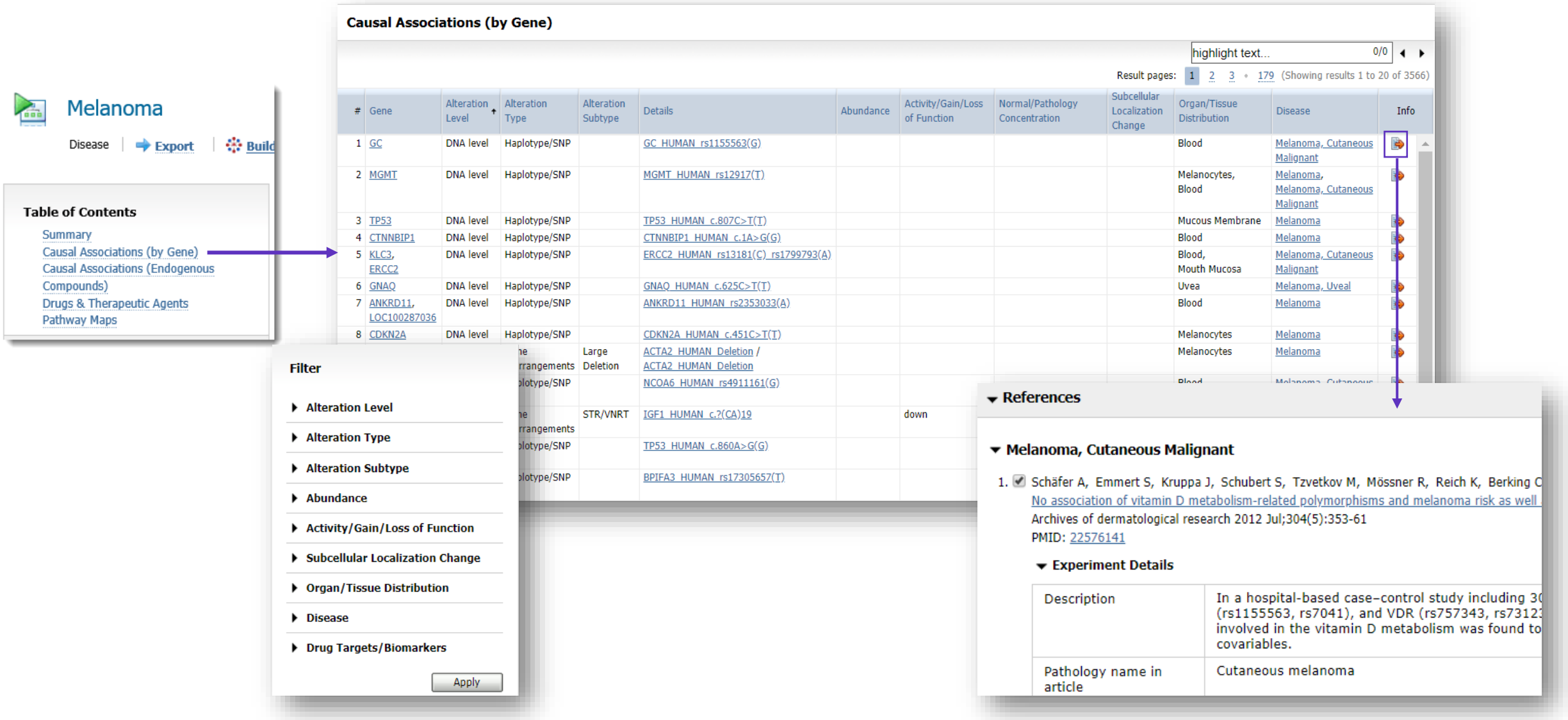
What can I learn about genes being aberrantly expressed in melanoma?



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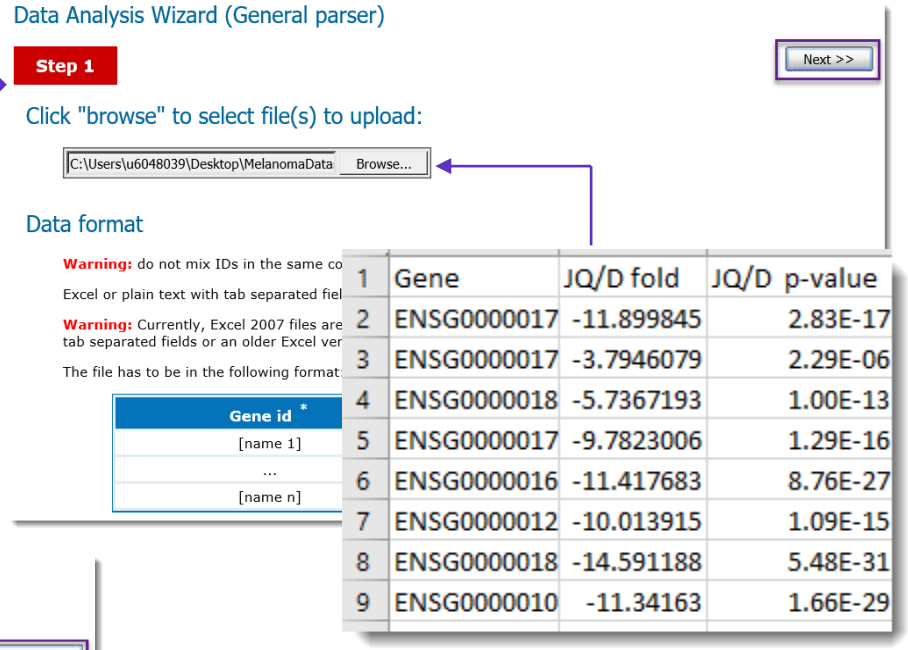
2. Uploading data

Upload data into MetaCore

1

2



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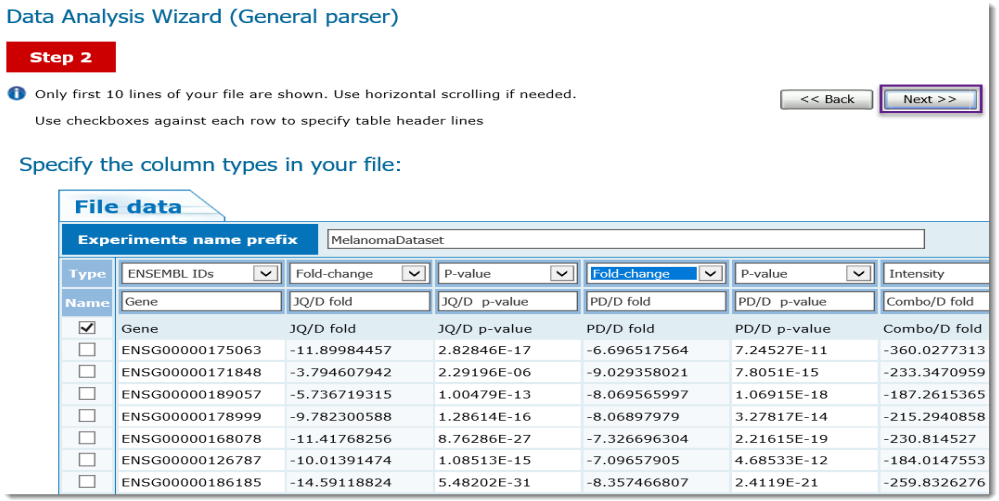

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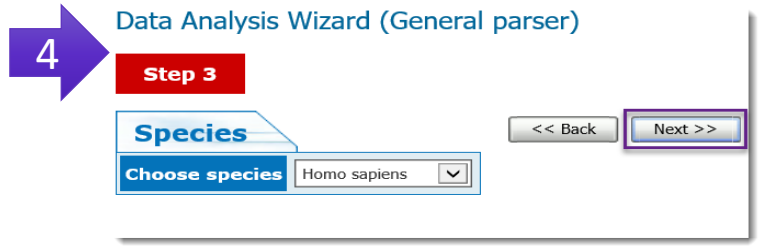

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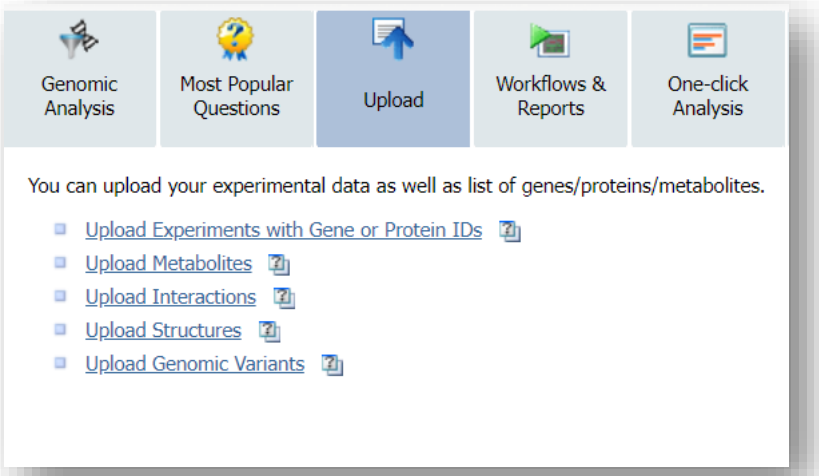
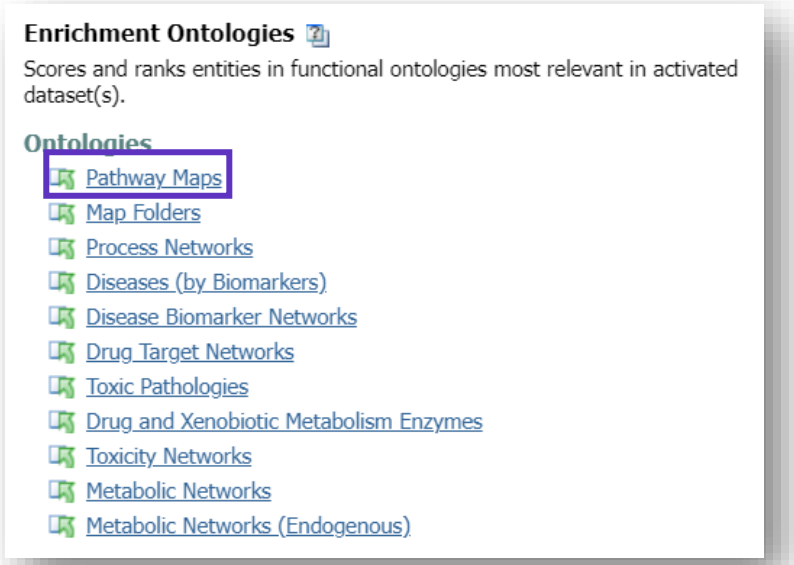
3. Pathway map enrichment

Which pathway maps are significantly enriched?

Upload dataset into Metacore

Analyze Pathway Maps





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

Experiments

Experiment name	Species	Network Objects
MelanomaDataset2_BETfold-change	Homo sapiens	474
MelanomaDataset2_MEKfold-change	Homo sapiens	398
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(pValue)

#	Maps	0 0.5 1 1.5 2 2.5 3 3.5 4 -log(pValue)	pValue	min(pValue)	FDR	Ratio
1	Aberrant B-Raf signaling in melanoma progression		3.694e-5 2.177e-5 2.255e-5	2.177e-5	1.359e-3 7.621e-4 1.597e-3	7/55 7/55 9/55
2	The role of aberrations in CDKN2 locus and CDK4 in familial melanoma		1.149e-2 8.773e-4 7.754e-3	8.773e-4	1.186e-1 1.663e-2 7.845e-2	3/28 4/28 4/28
3	FGF2 signaling in melanoma		4.140e-3 3.084e-3 4.763e-3	3.084e-3	6.145e-2 4.067e-2 5.912e-2	4/39 4/39 5/39
4	Upregulation of MITF in melanoma		3.084e-3 1.830e-2 3.344e-3	3.084e-3	4.923e-2 1.189e-1 4.793e-2	4/36 3/36 5/36

Map folder name

Significance of overlap of differentially expressed genes in the folder

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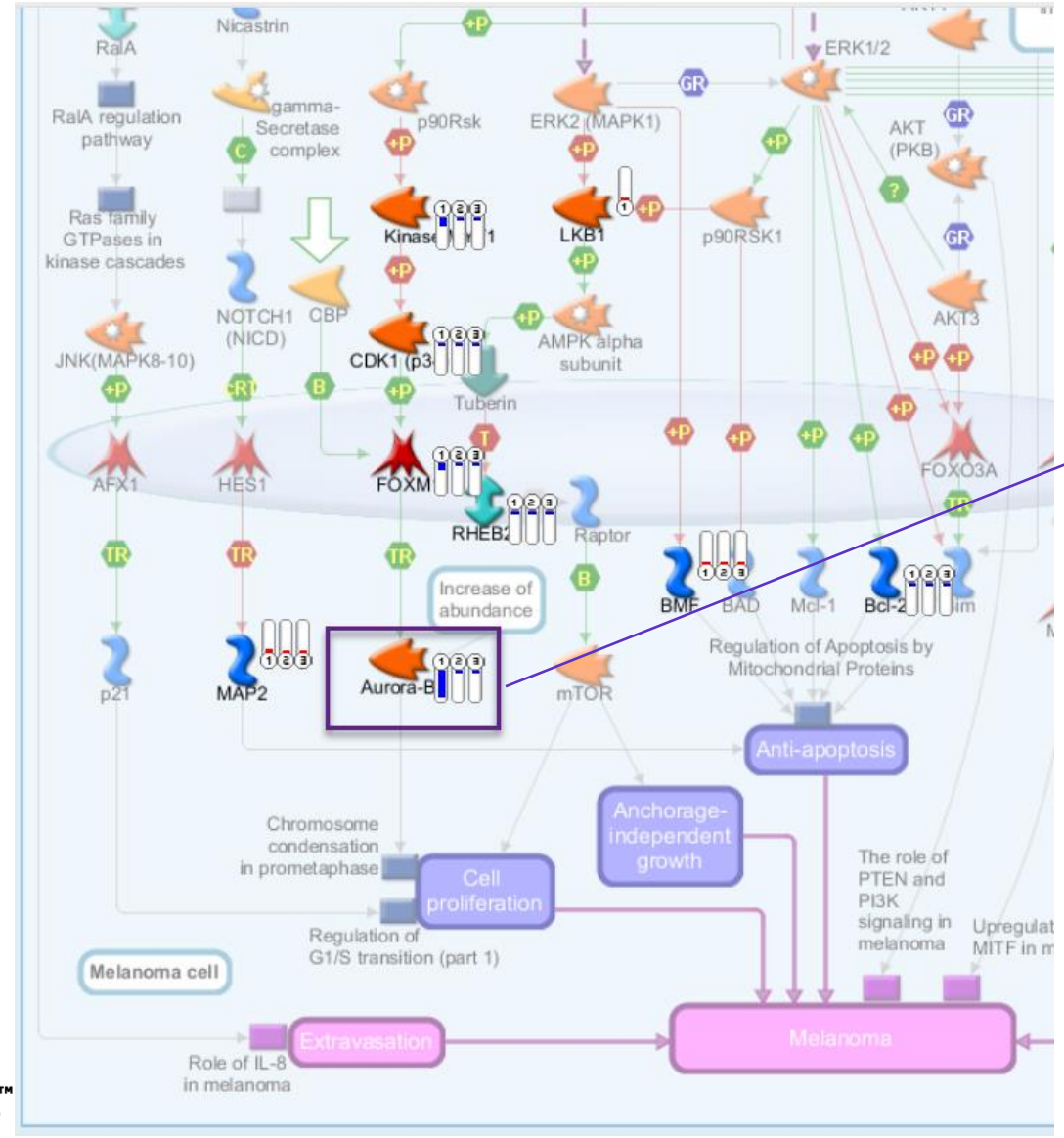
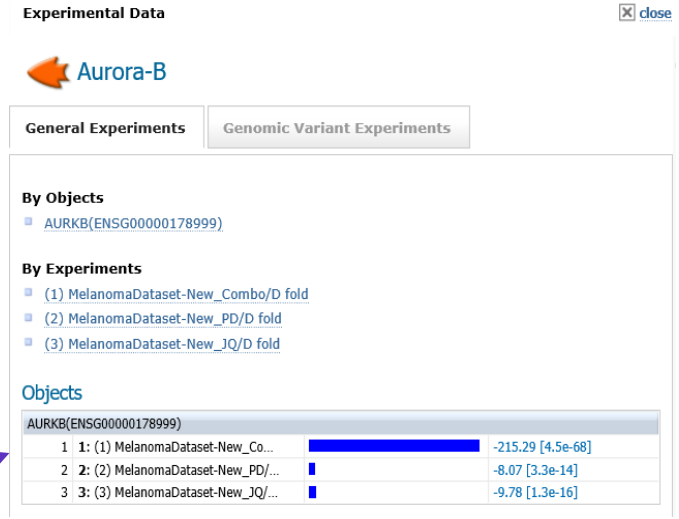
What pathways are disrupted by the differentially expressed genes?





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

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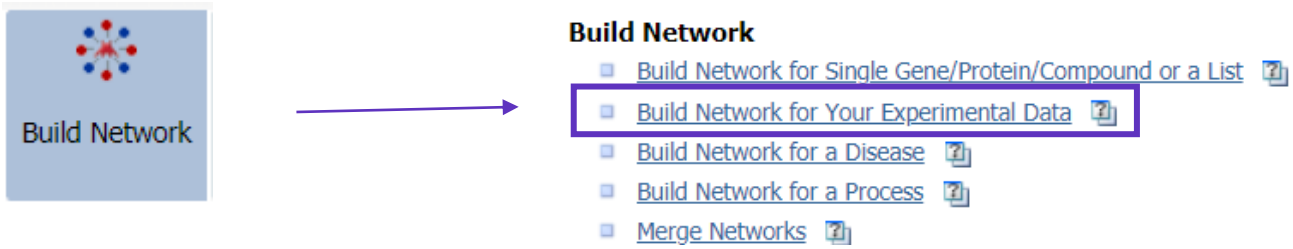
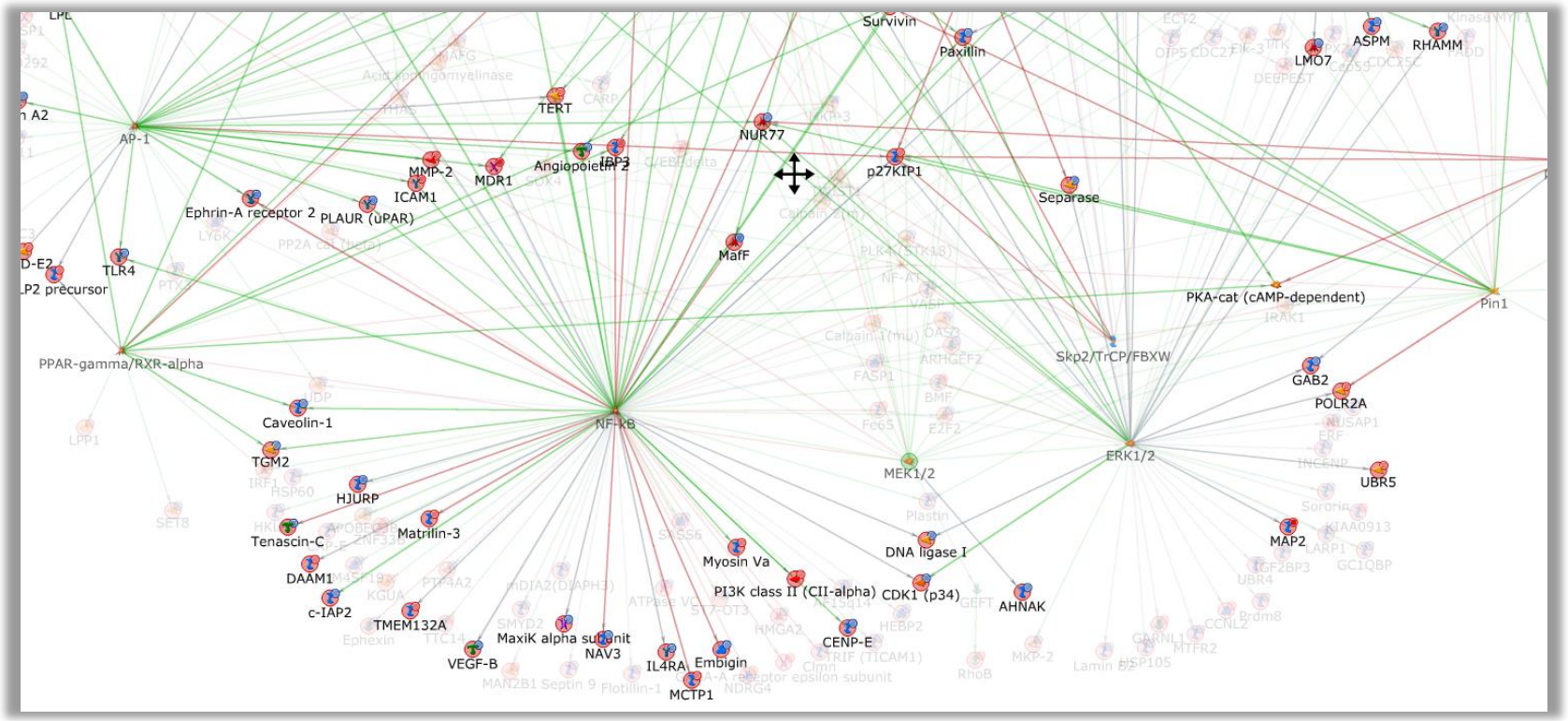
4. Building networks

Hypothesizing mechanisms of action behind MEK inhibitors by building network





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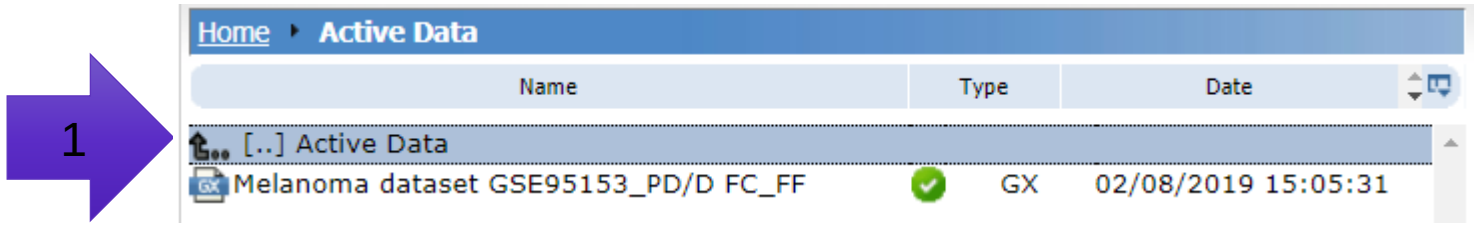
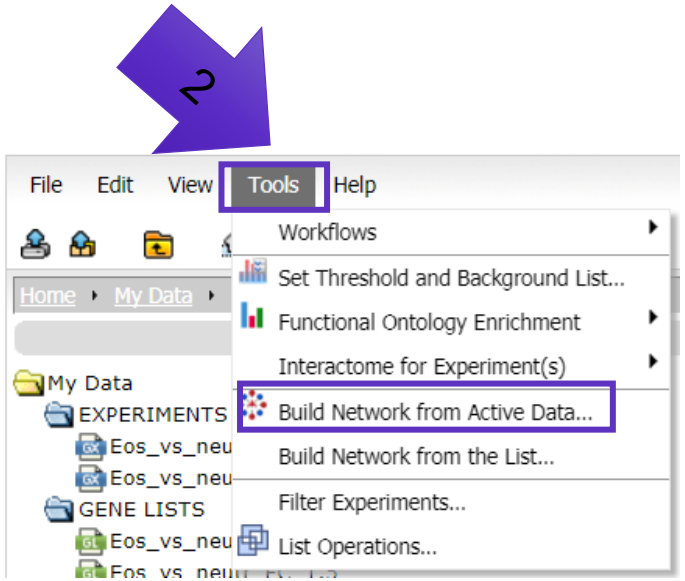
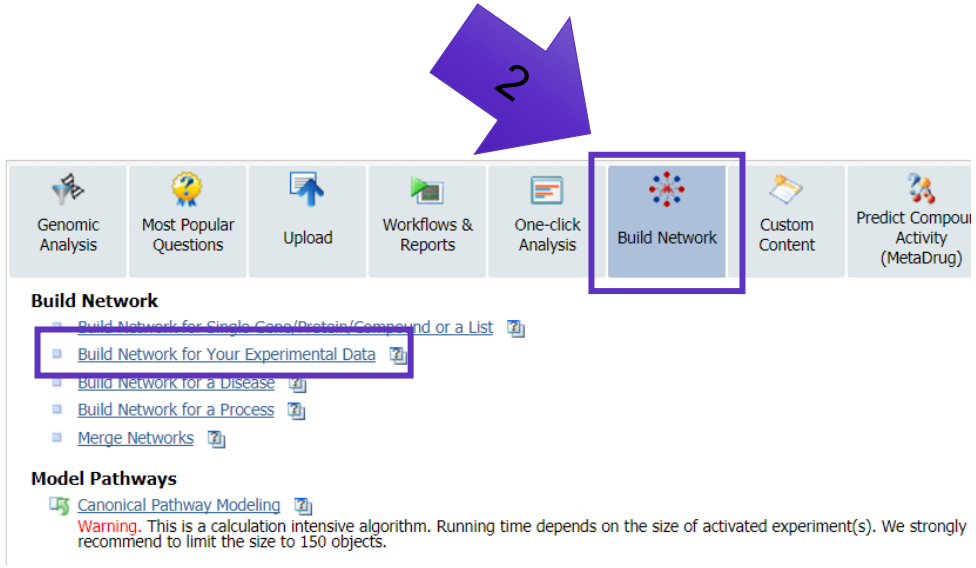
Create a network from your experimental data





OR



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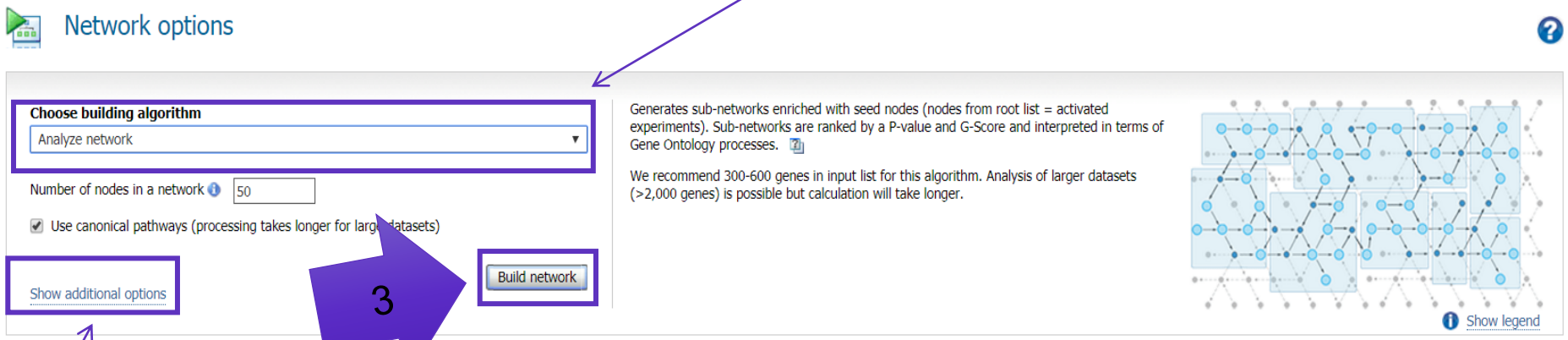
Create a network from your experimental data

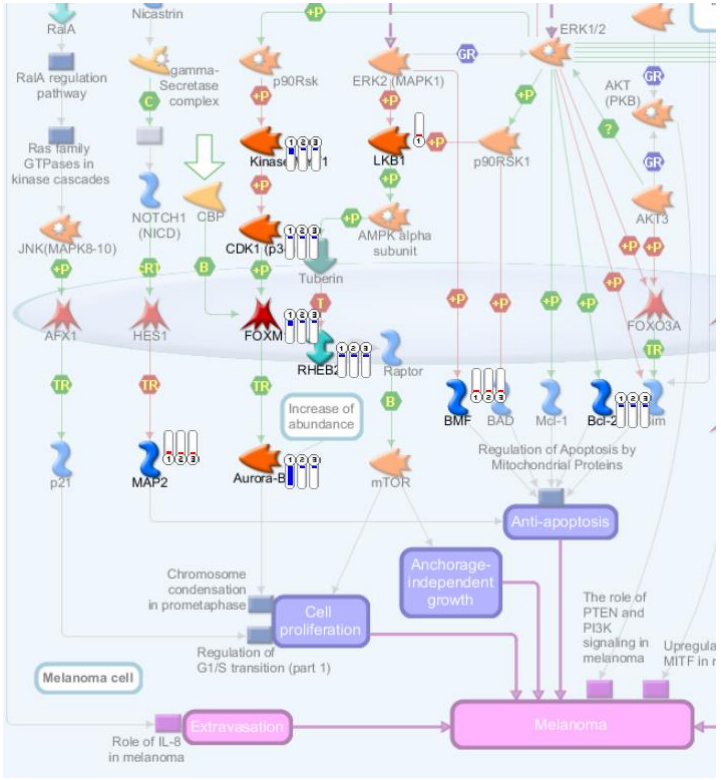
There are 10 building algorithms with short description and recommendations



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

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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!

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Questions?

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