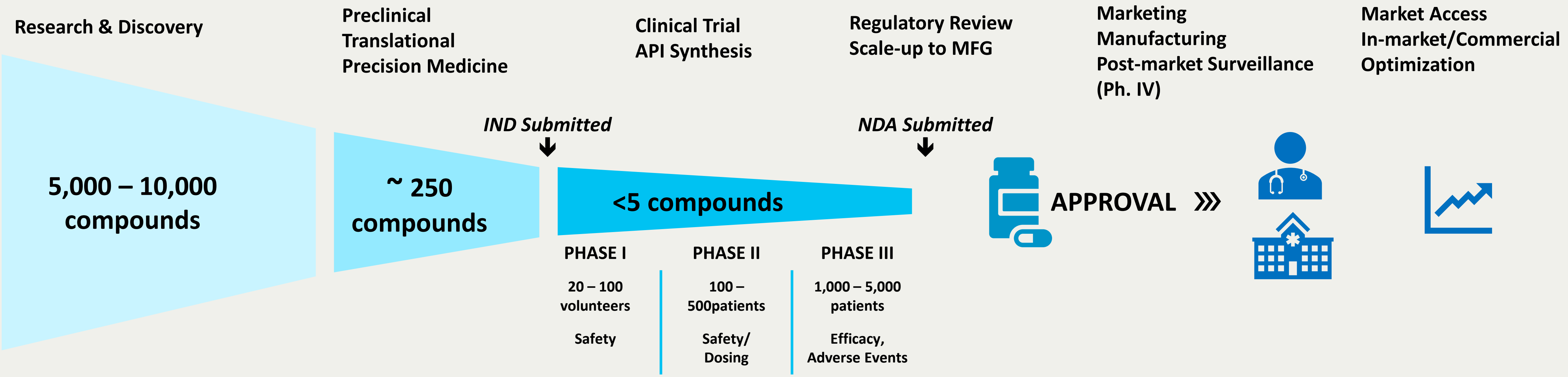
Clarivate
Cortellis™

MetaCore
Advanced Training Session

Kinsi Oberoi, Solution Scientist

4/13/2020

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



Research & Discovery

Preclinical
Translational
Precision Medicine

Clinical Trial
API Synthesis

Regulatory Review
Scale-up to MFG

Marketing
Manufacturing
Post-market Surveillance
(Ph. IV)

Market Access
In-market/Commercial
Optimization

PHASE I	PHASE II	PHASE III
20 – 100 volunteers	100 – 500patients	1,000 – 5,000 patients
Safety	Safety/ Dosing	Efficacy, Adverse Events

Web of Science | *Cortellis* | *Decision Resources Group*

Web of Science | **MetaCore** | **Drug Discovery** (formerly Integrity) | **Clinical Trials** | **CI & Deals, Timeline & Success Rates** | **Regulatory, CMC, PV, CIRS** | **Digital Health** | **Generics** (formerly Newport) | **Market Access** | **Multi-Channel Engagement** | ***Software Solutions***

Bioinformatics Knowledge Mgmt | **Drug Repurposing** | **Clinical Benchmarking** | **Asset Evaluation** | **Reg Strategy & Process** | **Predictive Data Sciences** | **HEOR & Access Strategy** | **Real-World Evidence** | ***Consulting***

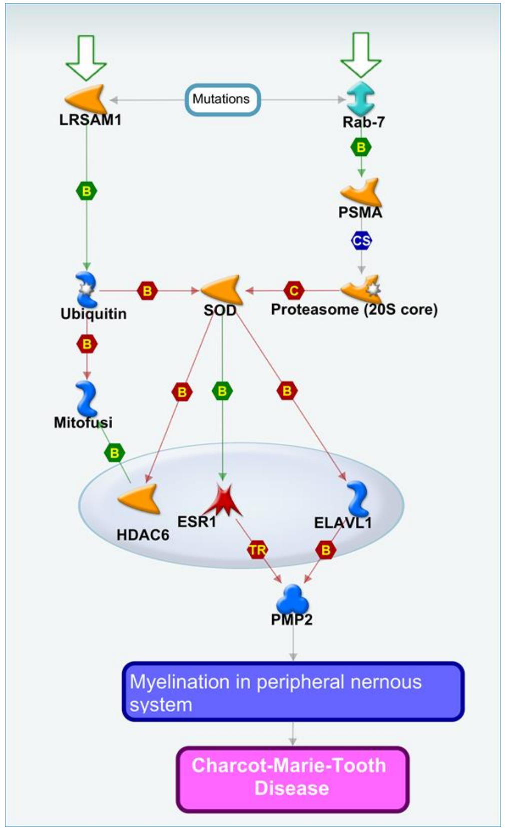
Data as a Service, APIs, Custom Data | **MDM, Ontologies, Data Lakes** | **Content as a Service** | ***Data***

Cortellis™

Agenda

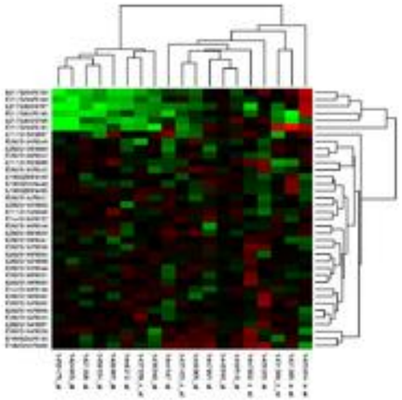
Metacore Training

- Metacore Overview with live demo session showing how to:
  - Introduction to Key Pathway Advisor
  - Analyzing multi-omics data (RNA-seq, proteomics, metabolomics, etc)
  - Q&A



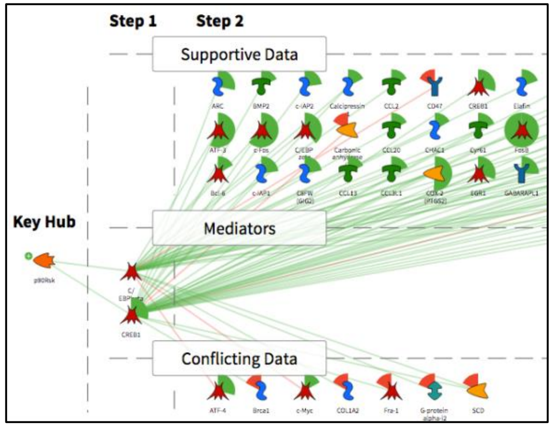
Key Pathway Advisor

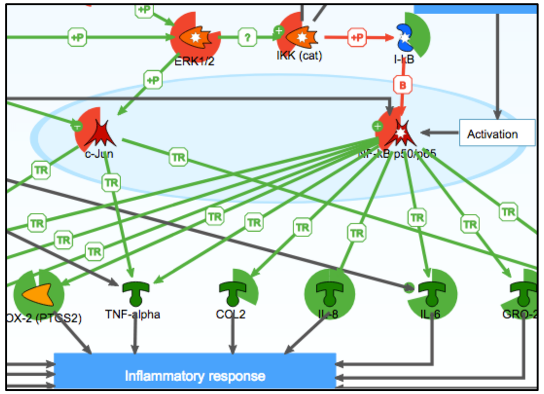
Key Pathway Advisor



Input
Differentially expressed genes

KPA





Output

- Key hubs regulating gene expression.
- Impact on pathway maps.

Gain molecular understanding of disease

Analyse expression data to in the context of validated biological interactions and pathways.

Generate causal networks and confirm hypotheses for targets and mechanisms of action

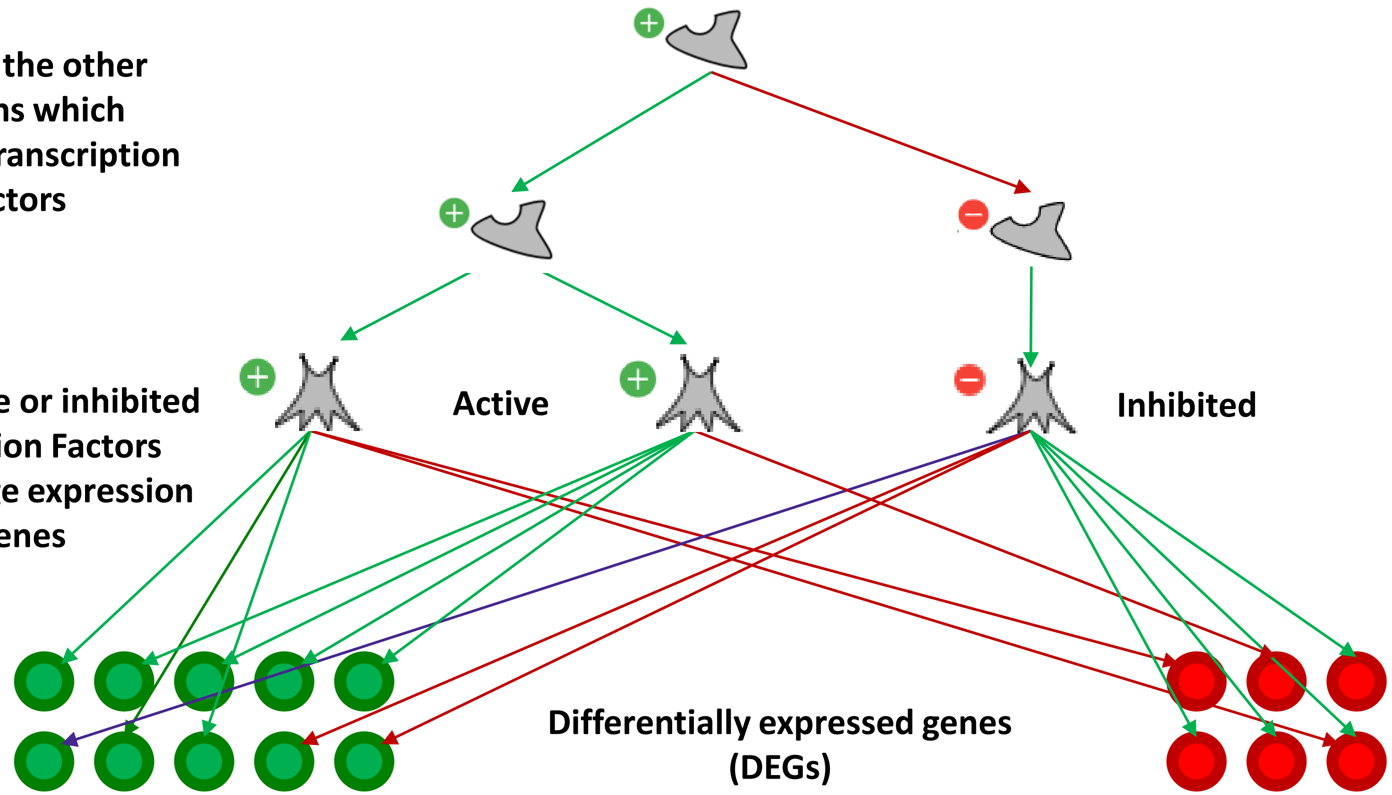
Predict key molecules in your data that may be causative for the changes observed (causal reasoning network analysis)

KEY HUBS

● Actived or Overconnected object

● Inhibited object

Power analytics – causal reasoning



Identify the other proteins which regulate Transcription Factors

Predict active or inhibited Transcription Factors which change expression of genes

Active

Inhibited

Differentially expressed genes (DEGs)

Up-regulated genes

Down-regulated genes

1. 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.
2. 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.

Prior knowledge

KEY HUBS

Actived or Overconnected object

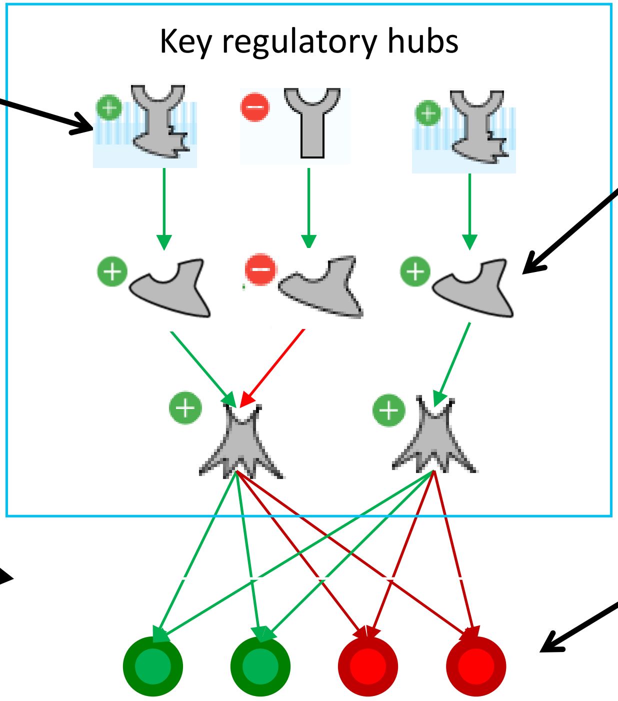
Inhibited object

Repositioning drug targets

Is this receptor already being targeted for a similar indication?

Comparing known biomarkers

Does my gene signature match what has been published already? Are the results consistent with my findings?



Differentially expressed genes (DEGs)

Novel drug targets

Is this kinase downstream of a known drug target?

Stratifying biomarkers

Has this gene been associated with other similar indications or is it unique to my indication?

Associate results with known drug targets and biomarkers

Cortellis™

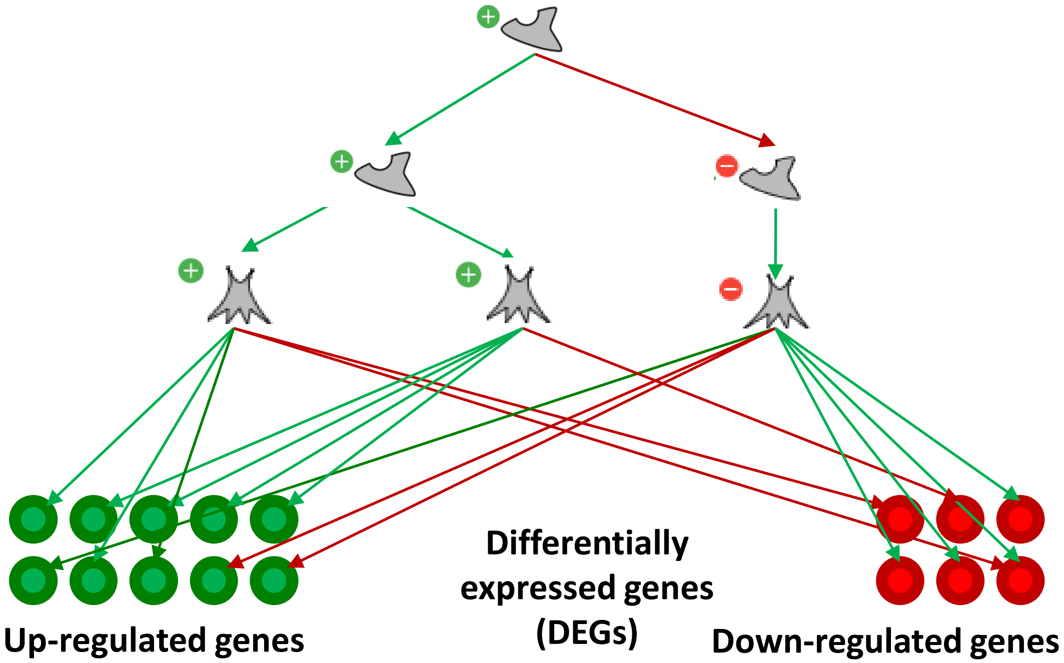
Powerful analytics – synergy enrichment

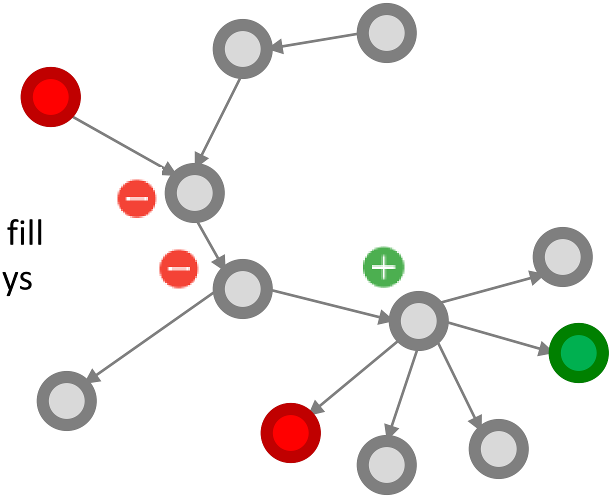
Up-stream analysis

Predict Key Hubs on molecular network which drive differential expression

Down-stream analysis

Identify Key Pathways affected by differential expression and aberrant signaling





Use Key Hubs to fill gaps on pathways

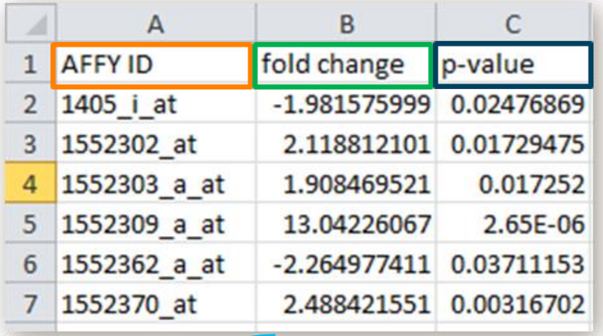
Formatting and uploading data

You can use the same identifiers as in MetaCore

Keep column titles simple

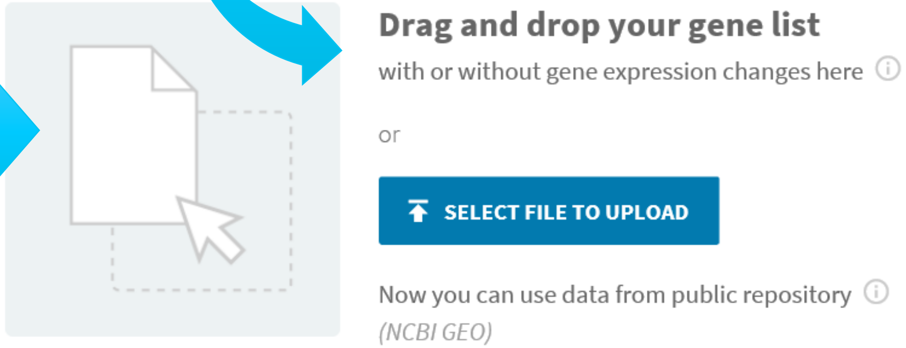
P-values can be included but are not required

1



	A	B	C
1	AFFY ID	fold change	p-value
2	1405_i_at	-1.981575999	0.02476869
3	1552302_at	2.118812101	0.01729475
4	1552303_a_at	1.908469521	0.017252
5	1552309_a_at	13.04226067	2.65E-06
6	1552362_a_at	-2.264977411	0.03711153
7	1552370_at	2.488421551	0.00316702

2

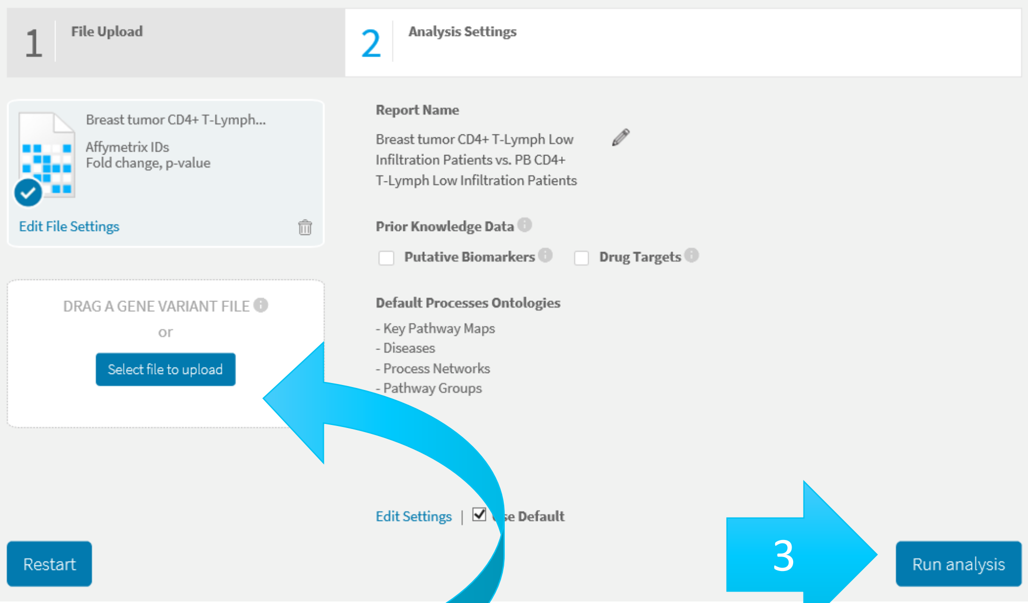


Drag and drop your gene list

with or without gene expression changes here ⓘ

or

Now you can use data from public repository ⓘ *(NCBI GEO)*



Breast tumor CD4+ T-Lymph...
Affymetrix IDs
Fold change, p-value

Report Name

Breast tumor CD4+ T-Lymph Low Infiltration Patients vs. PB CD4+ T-Lymph Low Infiltration Patients

Prior Knowledge Data

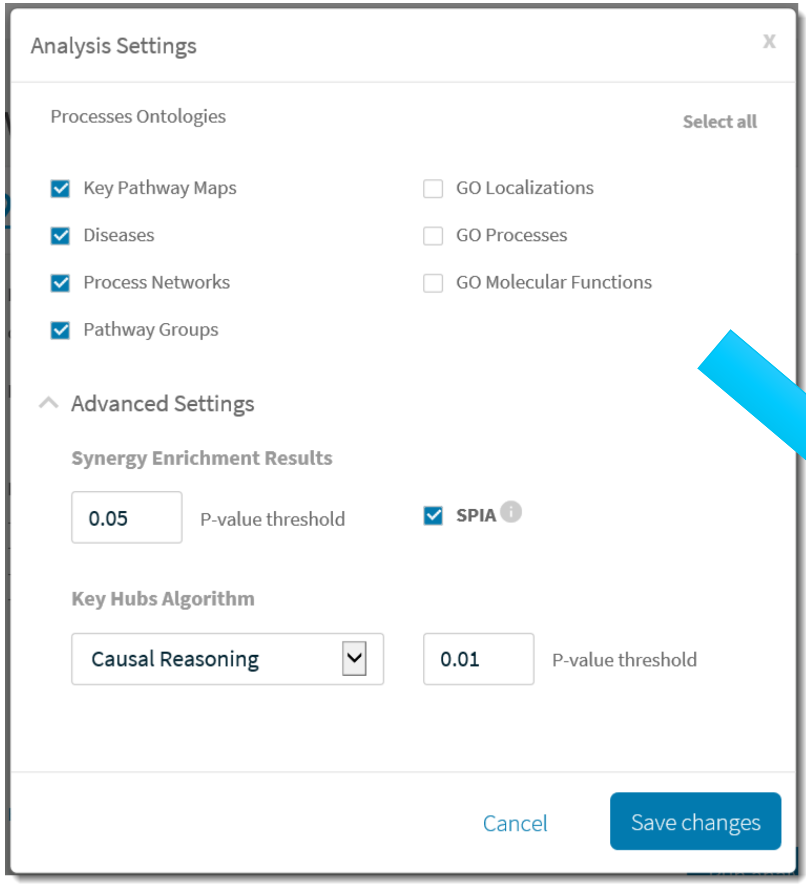
☐ **Putative Biomarkers** ☐ **Drug Targets**

Default Processes Ontologies

- Key Pathway Maps
- Diseases
- Process Networks
- Pathway Groups

3

Analysis Settings



Analysis Settings

Processes Ontologies

☑ Key Pathway Maps
☑ Diseases
☑ Process Networks
☑ Pathway Groups
☐ GO Localizations
☐ GO Processes
☐ GO Molecular Functions

Advanced Settings

Synergy Enrichment Results

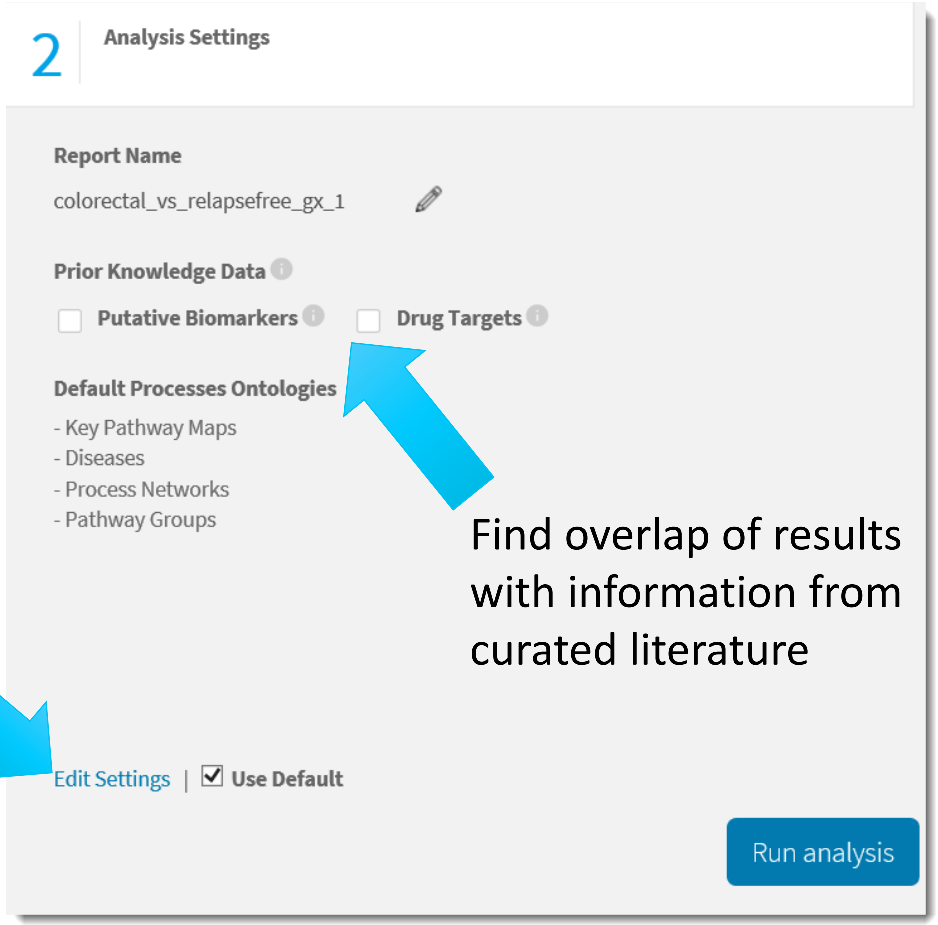
0.05 P-value threshold

☑ **SPIA**

Key Hubs Algorithm

Causal Reasoning

0.01 P-value threshold



2 **Analysis Settings**

Report Name

colorectal_vs_relapsefree_gx_1

Prior Knowledge Data

☐ **Putative Biomarkers** ☐ **Drug Targets**

Default Processes Ontologies

- Key Pathway Maps
- Diseases
- Process Networks
- Pathway Groups

Edit Settings | ☑ **Use Default**

Find overlap of results with information from curated literature

Use HTML Interface to export results


colorectal_vs_relapsefree_gx_1

Status **Complete** - view as HTML | PDF | XLS

19:10:09 • 20 JUN 2018

Questions:

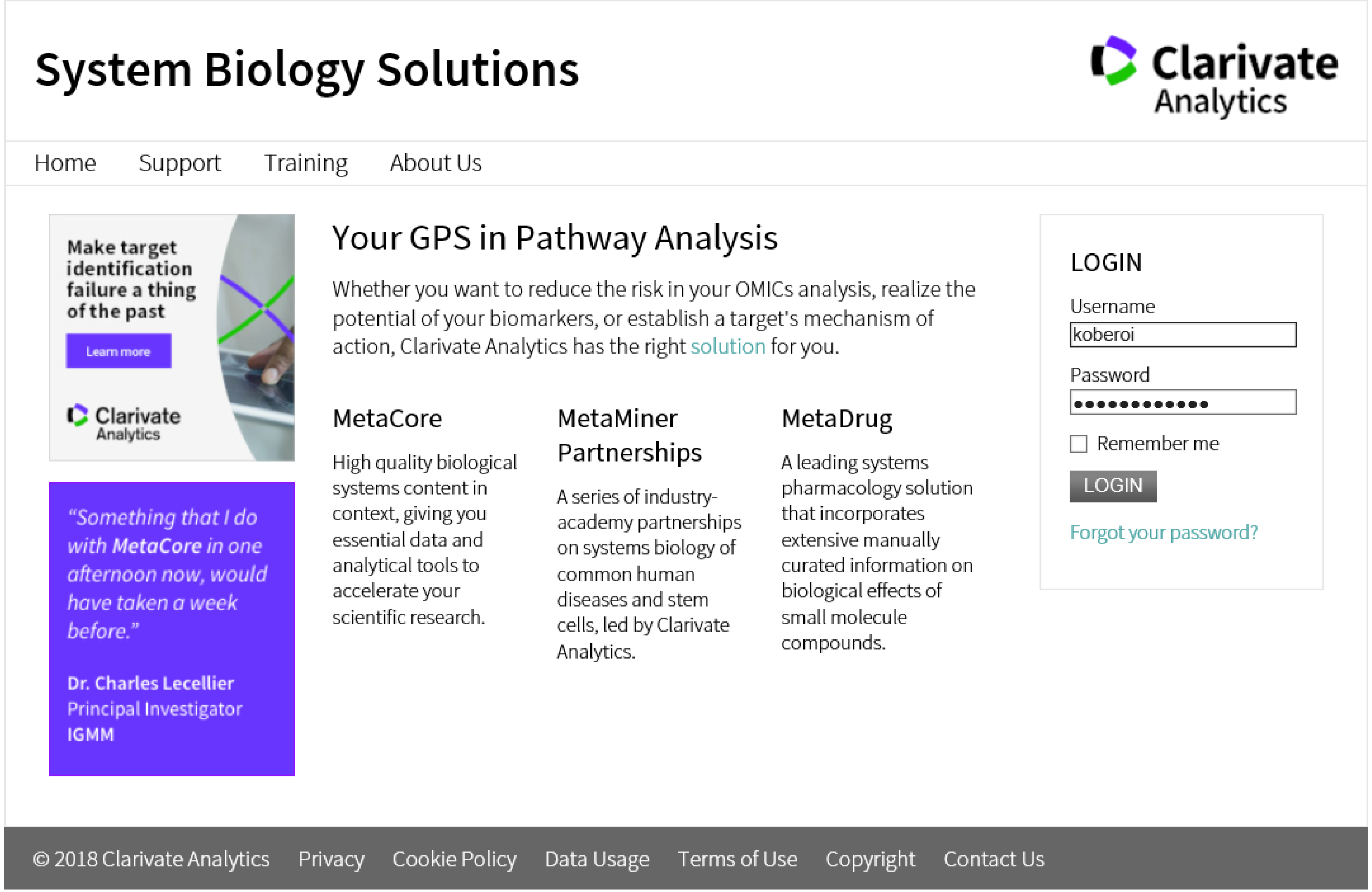
- What Key pathways are linked with the unique differentially expresses genes from Triple negative breast cancer?

- What direct and indirect regulators could be responsible for the unique gene signature for Triple negative breast cancer dataset?

Multi-Omics Analysis

Metacore Login Page

https://portal.genego.com/



System Biology Solutions

Clarivate Analytics

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.

> *"Something that I do with **MetaCore** in one afternoon now, would have taken a week before."*
>
> **Dr. Charles Lecellier**
> Principal Investigator
> **IGMM**

LOGIN

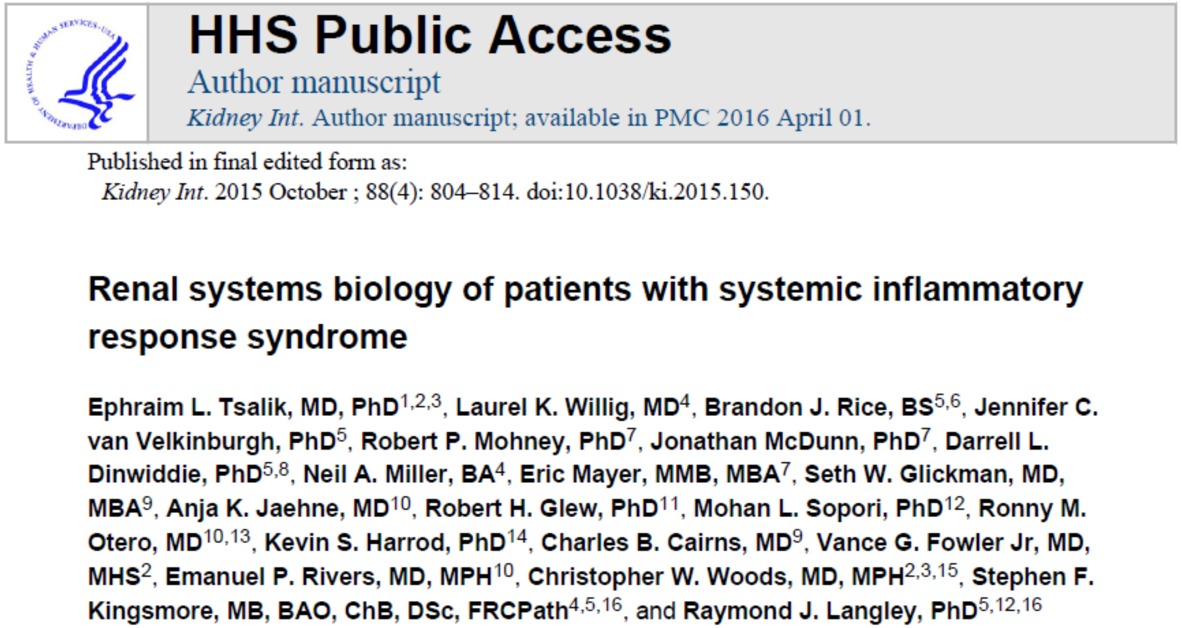
Username: koberoi

Password: ●●●●●●●●●●●●

☐ Remember me

Multi-omics analysis in MetaCore. Use case

- Cohort of 150 patients from CAPSOD study with varying renal dysfunction in patients with sepsis or pneumonia.
- Renal dysfunction was classified using the Acute Kidney Injury Network (AKIN) criteria.
    - AKI0 (no significant increase in serum creatinine) n=65
    - AKI1 (serum creatinine increase of ≥ 0.3 mg/dl, or 150% to 200% above baseline) n=41
    - AKI2/3 (serum creatinine increase more that 200% above baseline, or ≥ 4.0 mg/dl with an acute increase of at least 0.5 mg/dl) n=20
    - Chronic hemodialysis (HD) n=24



HHS Public Access

Author manuscript

Kidney Int. Author manuscript; available in PMC 2016 April 01.

Published in final edited form as:
Kidney Int. 2015 October ; 88(4): 804–814. doi:10.1038/ki.2015.150.

Renal systems biology of patients with systemic inflammatory response syndrome

Ephraim L. Tsalik, MD, PhD[1,2,3], **Laurel K. Willig, MD**[4], **Brandon J. Rice, BS**[5,6], **Jennifer C. van Velkinburgh, PhD**[5], **Robert P. Mohney, PhD**[7], **Jonathan McDunn, PhD**[7], **Darrell L. Dinwiddie, PhD**[5,8], **Neil A. Miller, BA**[4], **Eric Mayer, MMB, MBA**[7], **Seth W. Glickman, MD, MBA**[9], **Anja K. Jaehne, MD**[10], **Robert H. Glew, PhD**[11], **Mohan L. Sopori, PhD**[12], **Ronny M. Otero, MD**[10,13], **Kevin S. Harrod, PhD**[14], **Charles B. Cairns, MD**[9], **Vance G. Fowler Jr, MD, MHS**[2], **Emanuel P. Rivers, MD, MPH**[10], **Christopher W. Woods, MD, MPH**[2,3,15], **Stephen F. Kingsmore, MB, BAO, ChB, DSc, FRCPath**[4,5,16], and **Raymond J. Langley, PhD**[5,12,16]

Multi-omics analysis in MetaCore. Use case dataset

- -Mass spectrometry was used to measure the levels of 370 plasma metabolites
  - 241 metabolites were annotated
  - Clinical assays of serum creatine, capillary lactate, and serum glucose was used to validate the use of the MS data in a semiquantitative fashion.
  - 138 annotated metabolites were significantly different from the AKI0 control group using ANOVA with 1% false discovery rate correction.
- -Mass spectrometry was used to measure the levels of plasma proteins
  - 164 proteins were identified using peptide sequences
  - 46 were significantly different from the AKI0 control group using ANOVA with 5% false discovery rate correction.
- -RNA-seq was used to measure the blood transcriptome
  - 133 out of 150 patients were used due to poor insufficient quality.
  - 1,997 genes were significantly differentially expressed across all groups using ANOVA with 1% false discovery rate correction.

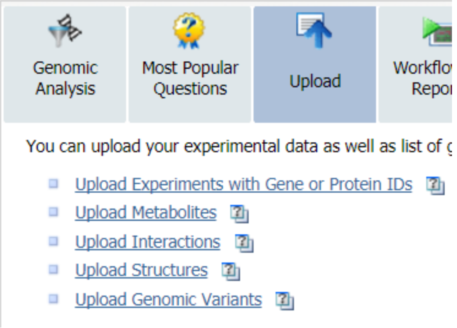
Multi-omics analysis in MetaCore

Upload your omics data

Analyse your data

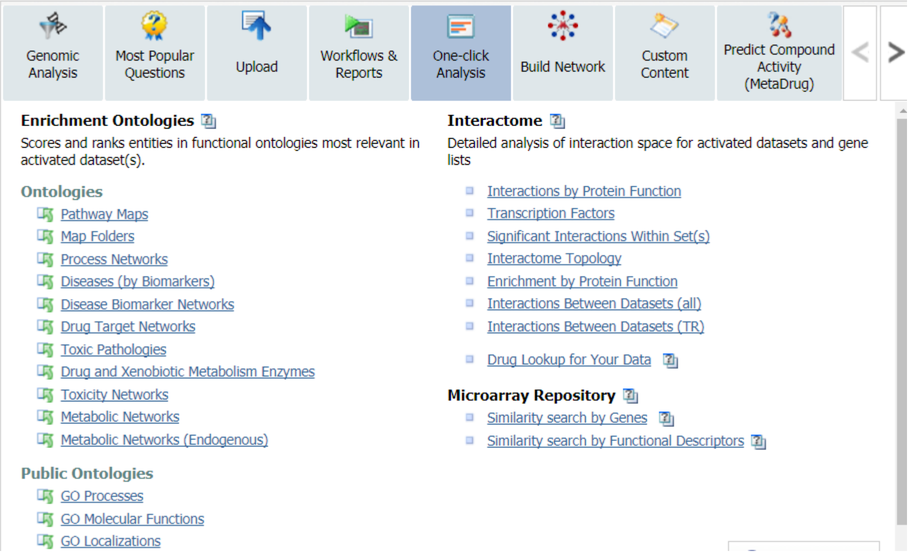
Upload

One-click Analysis



You can upload your experimental data as well as list of

- Upload Experiments with Gene or Protein IDs
- Upload Metabolites
- Upload Interactions
- Upload Structures
- Upload Genomic Variants



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)

Public Ontologies

- GO Processes
- GO Molecular Functions
- GO Localizations

Interactome

Detailed analysis of interaction space for activated datasets and gene lists

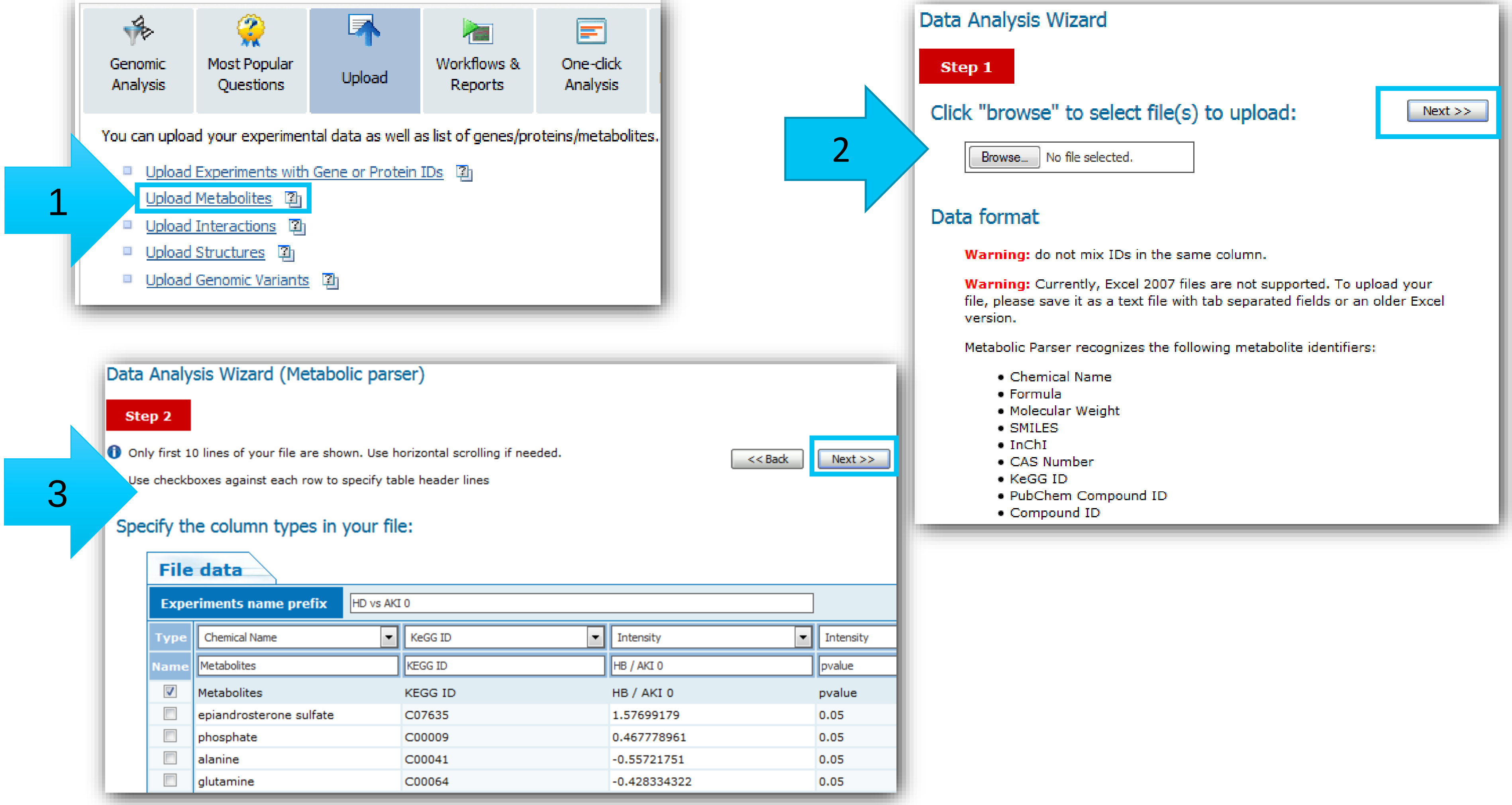
- Interactions by Protein Function
- Transcription Factors
- Significant Interactions Within Set(s)
- Interactome Topology
- Enrichment by Protein Function
- Interactions Between Datasets (all)
- Interactions Between Datasets (TR)

- Drug Lookup for Your Data

Microarray Repository

- Similarity search by Genes
- Similarity search by Functional Descriptors

Upload metabolomic data



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
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- Upload Genomic Variants

Data Analysis Wizard

Step 1

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

No file selected.

Data format

Warning: do not mix IDs in the same column.

Warning: Currently, Excel 2007 files are not supported. To upload your file, please save it as a text file with tab separated fields or an older Excel version.

Metabolic Parser recognizes the following metabolite identifiers:

- Chemical Name
- Formula
- Molecular Weight
- SMILES
- InChI
- CAS Number
- KeGG ID
- PubChem Compound ID
- Compound ID

Data Analysis Wizard (Metabolic 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:

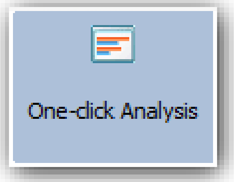
File data

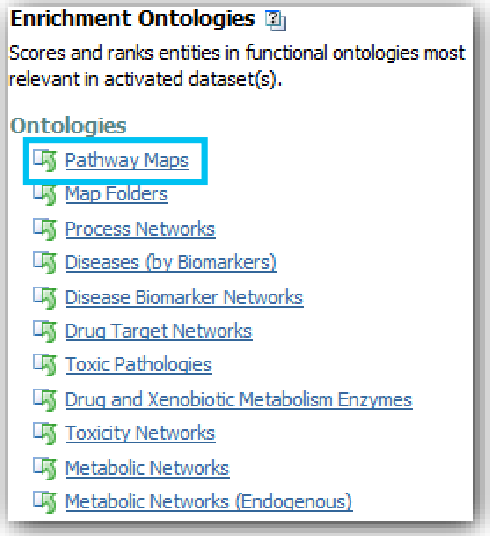
Experiments name prefix: HD vs AKI 0

Type	Chemical Name	KeGG ID	Intensity	Intensity
Name	Metabolites	KEGG ID	HB / AKI 0	pvalue
☑	Metabolites	KEGG ID	HB / AKI 0	pvalue
☐	epiandrosterone sulfate	C07635	1.57699179	0.05
☐	phosphate	C00009	0.467778961	0.05
☐	alanine	C00041	-0.55721751	0.05
☐	glutamine	C00064	-0.428334322	0.05

Find pathways where the metabolic and proteomic data are both involved

Enrichment analysis





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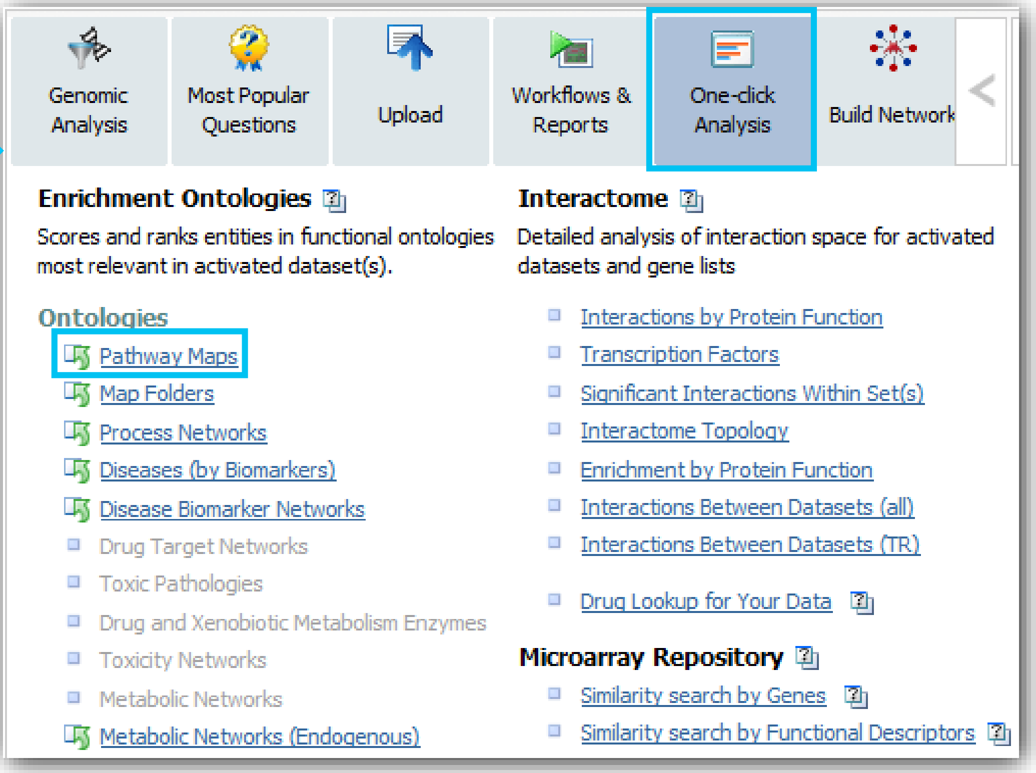
- Drug and Xenobiotic Metabolism Enzymes
- Toxicity Networks
- Metabolic Networks
- Metabolic Networks (Endogenous)

Find pathways where the metabolic and proteomic data are both involved

1

Name		Type	Date
[..] Active Data			
AKI1 vs AKI0	✓	MX	08/17/2017 14:47:55
AKI2-3 vs AKI0	✓	MX	08/17/2017 14:48:30
HD vs AKI 0	✓	MX	08/17/2017 14:49:15
AKI1 vs AKI0 prot	✓	GX	08/17/2017 14:55:53
AKI2-3 vs AKI0 prot	✓	GX	08/17/2017 14:56:50
HD vs AKI0 prot	✓	GX	08/17/2017 14:57:19

2



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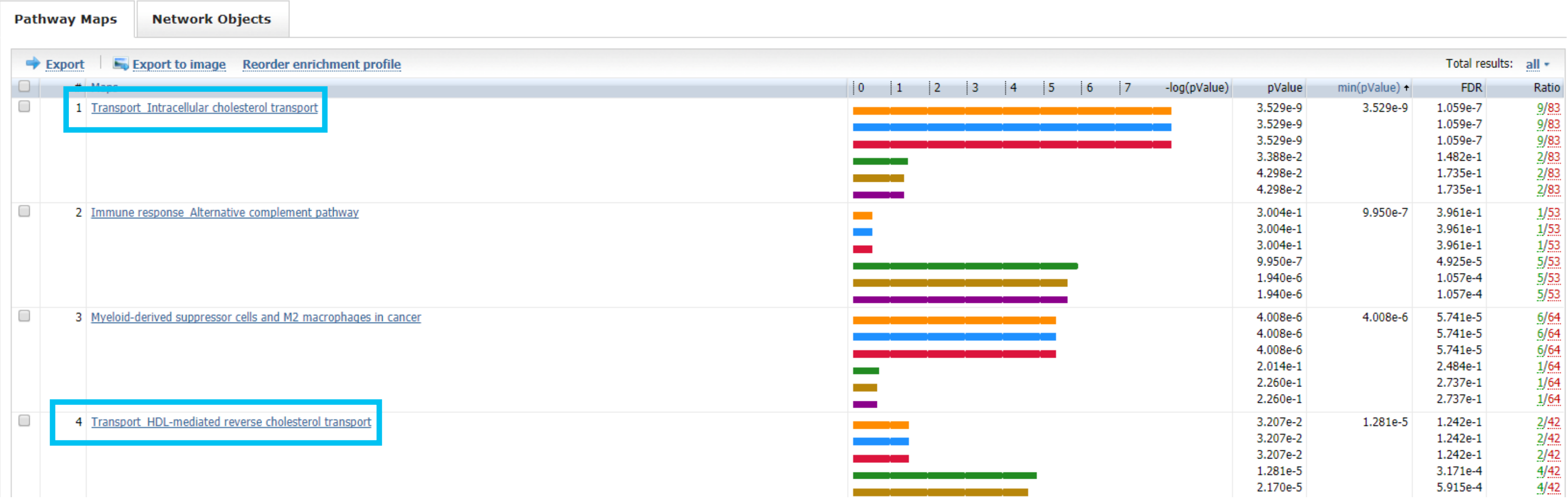
Find pathways where the metabolic and proteomic data are both involved

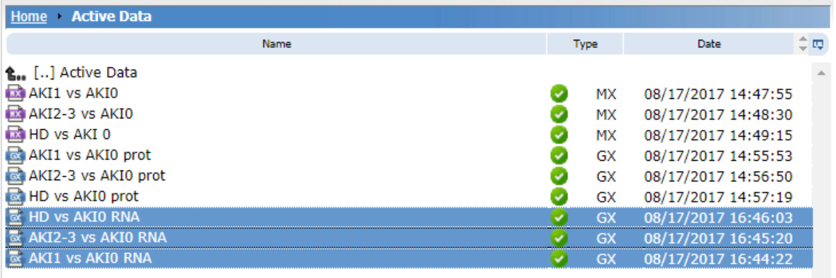


☐	#	Maps	-log(pValue)	pValue	min(pValue)	FDR	Ratio
☐	1	Transport_Intracellular cholesterol transport		3.529e-9	3.529e-9	1.059e-7	9/83
				3.529e-9		1.059e-7	9/83
				3.529e-9		1.059e-7	9/83
				3.388e-2		1.482e-1	2/83
				4.298e-2		1.735e-1	2/83
				4.298e-2		1.735e-1	2/83
☐	2	Immune response_Alternative complement pathway		3.004e-1	9.950e-7	3.961e-1	1/53
				3.004e-1		3.961e-1	1/53
				3.004e-1		3.961e-1	1/53
				9.950e-7		4.925e-5	5/53
				1.940e-6		1.057e-4	5/53
				1.940e-6		1.057e-4	5/53
☐	3	Myeloid-derived suppressor cells and M2 macrophages in cancer		4.008e-6	4.008e-6	5.741e-5	6/64
				4.008e-6		5.741e-5	6/64
				4.008e-6		5.741e-5	6/64
				2.014e-1		2.484e-1	1/64
				2.260e-1		2.737e-1	1/64
				2.260e-1		2.737e-1	1/64
☐	4	Transport_HDL-mediated reverse cholesterol transport		3.207e-2	1.281e-5	1.242e-1	2/42
				3.207e-2		1.242e-1	2/42
				3.207e-2		1.242e-1	2/42
				1.281e-5		3.171e-4	4/42
				2.170e-5		5.915e-4	4/42

- Cholesterol-related pathways appear as relevant

Overlay RNA-seq data to complete the picture

3


Home ▸ Active Data

Name		Type	Date
[..] Active Data			
AKI1 vs AKI0	✓	MX	08/17/2017 14:47:55
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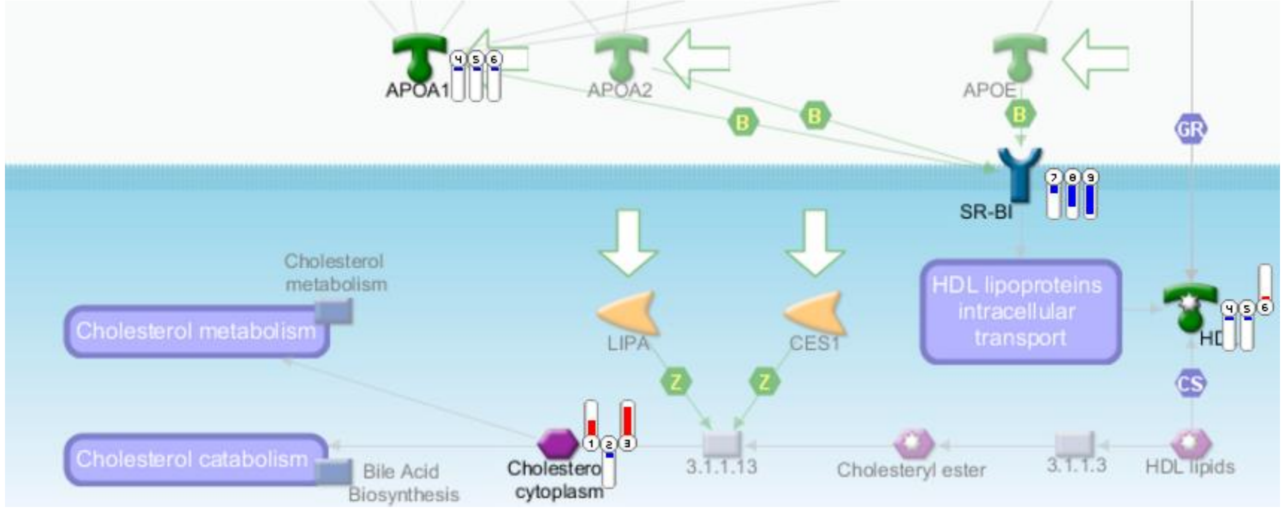
HD vs AKI 0	✓	MX	08/17/2017 14:49:15
AKI1 vs AKI0 prot	✓	GX	08/17/2017 14:55:53
AKI2-3 vs AKI0 prot	✓	GX	08/17/2017 14:56:50
HD vs AKI0 prot	✓	GX	08/17/2017 14:57:19
HD vs AKI0 RNA	✓	GX	08/17/2017 16:46:03
AKI2-3 vs AKI0 RNA	✓	GX	08/17/2017 16:45:20
AKI1 vs AKI0 RNA	✓	GX	08/17/2017 16:44:22

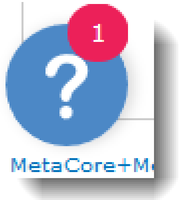
4

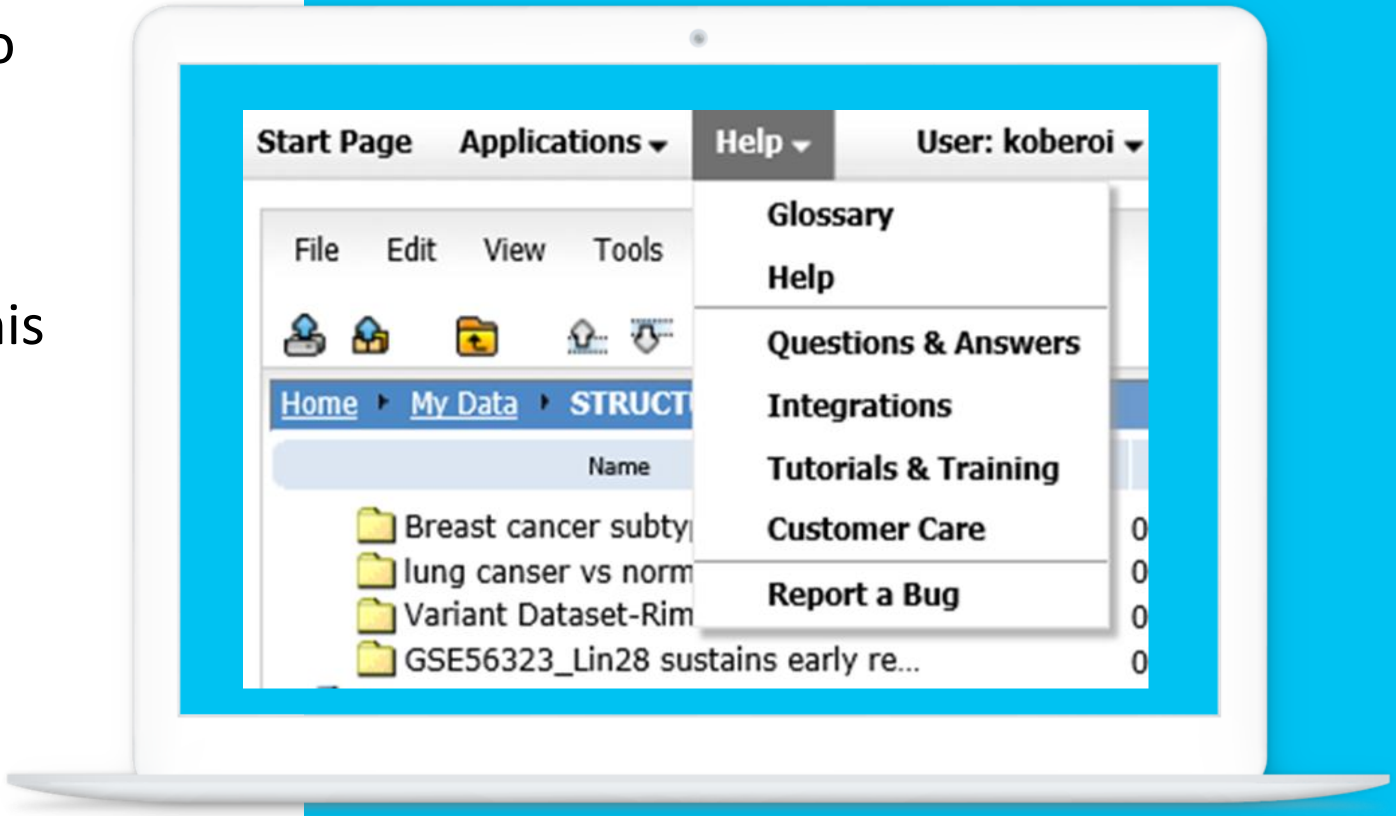


- Generate your hypothesis

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 this month to help deliver a great product experience





Screen caption

Cortellis™

A Clarivate Analytics solution

Thank you

Kinsi Oberoi
Kinsi.oberoi@Clarivate.com