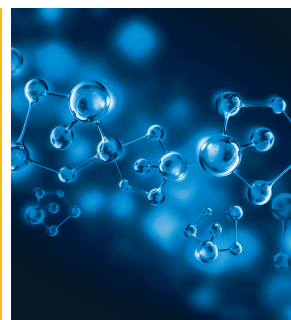# KEY PATHWAY ADVISOR (KPA)

POWERED BY THOMSON REUTERS METACORE™

KPA HIGHLIGHTS

- Simplifies 'omics data analysis
- Performs causal reasoning network analysis and applies a comprehensive pathway analysis workflow
- Enables gene expression and gene variant data integration
- Generates interactive structured reports for further analysis or sharing

WHO CAN BENEFIT

- Discovery biologists, including those without bioinformatics experience
- Bioinformaticians
- Pre-clinical scientists
- Translational researchers

Key Pathway Advisor on MetaCore accelerates your gene expression research and helps your organization spark innovation in patient stratification, disease mechanism reconstruction, target and biomarker discovery, and pharmacogenomics.

No bioinformatics experience required. In just a few clicks, KPA delivers the biological insight you need.

COMPREHENSIVE PATHWAY ANALYSIS

Gene expression analysis workflow is generally focused on identification of genes whose expression differs between two conditions (case/control studies) and pathways affected by defined genes. However, differential gene expression itself in turn could be the result of aberrant cellular signal transduction (due to environmental factors or gene variants with protein function impact).

KPA uses **causal reasoning network analysis** to predict Key Hubs transcriptional factors activity change (and their upstream regulators) that cause differential gene expression change. To perform this analysis, KPA leverages more than 100,000 manually annotated high-quality protein/RNA/compound interactions (including more than 34,000 transcriptional regulation interactions) stored in Thomson Reuters MetaBase™.

KPA also uses **synergy pathway analysis** to automatically define processes and pathway maps enriched with both experimentally defined and predicted Key Hubs gene sets in order to show connected, biologically relevant results.

INTEGRATED 'OMICS DATA ANALYSIS

KPA enables faster, more intuitive analysis of gene expression and associated gene variant data. Using MetaCore's Genomic Analysis Tools (GAT)*, you can annotate your experimentally defined gene variant list and narrow it down to as many as 150 of the most promising protein function impact variants.

The resulting list can be uploaded into KPA with expression data in order to identify pathway impact and hypothesize about gain and loss of function effect (e.g., if a missense mutation occurred on a statistically significant active Key Hub, it may indicate gain of function effect).

SIMPLE, INTUITIVE INTERFACE

Simply import your data into the program and apply default analytical parameters. KPA automatically calculates a comprehensive workflow and delivers your results in structured reports:

- Online interactive reports – browse **enrichment distributions, pathway maps,** and **significant molecular components**.

- PDF report – shows static lists of **enrichment distributions** and top ten pathway map pictures overlaid with significant molecular components. Ideal for showing pathway snapshots and distributions to your colleagues.

- XLS report – contains **expanded lists of molecular components** and cross-references between them. Allows you to sort/filter all molecules on the basis of various molecular characteristics, narrowing down your data and making them appropriate for use in the other system biology tools and workflows.

KPA AND METACORE: INTUITIVE TOOLS FOR 'OMICS RESEARCH

Powered by Thomson Reuters MetaCore, Key Pathway Advisor (KPA) is a Web application that allows you to submit gene expression data and apply a comprehensive workflow that analyzes data in both upstream and downstream directions. Like a biological version of the GPS in your car, KPA doesn't just visualize all possible pathways, it uses causal reasoning to point you to the most promising "routes," analyzing the key pathways activated in your data and showing the key genes or proteins driving the distribution of your data. **KPA can be added to any MetaCore subscription.**

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KPA ANALYSIS APPROACH

Predict Key Hubs and their activity on molecular interaction network which drive differential expression changes

Activation — Receptor — **Inhibition**

Enzymes

Transcriptional Factors

Differentially expressed genes

UPSTREAM ANALYSIS
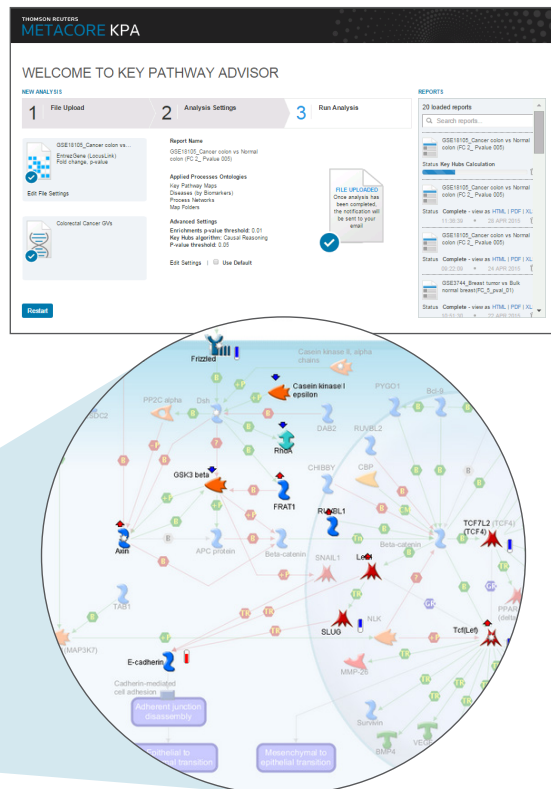
DOWNSTREAM ANALYSIS

Identify Key Pathways affected by differential expression and deregulated Key Hubs
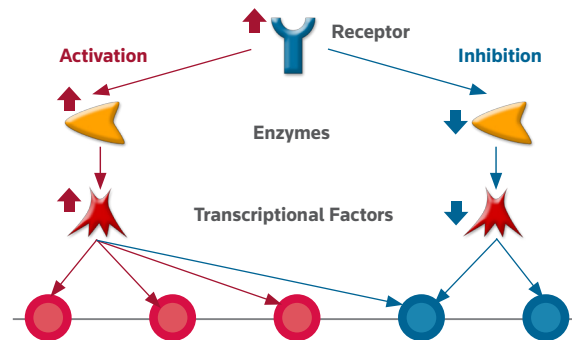
#	Name	Input Objects p-value	Key Hubs p-value	Union Objects p-value	stacked / grouped
1	Cell cycle_Role of APC in cell cycle regulation	2.763E-8	6.944E-4	5.605E-10	
2	Development_WNT signaling pathway. Part 2	1.41E-3	1.697E-8	7.332E-10	
3	IGF family signaling in colorectal cancer	3.648E-8	5.43E-4	1.169E-8	
4	Cytoskeleton remodeling_TGF, WNT and cytoskeletal remodeling	8.263E-7	8.075E-5	2.453E-8	
5	Development_Regulation of epithelial-to-mesenchymal transition (EMT)	1.849E-5	9.178E-4	4.571E-8	
6	Some pathways of EMT in cancer cells	4.524E-5	2.473E-5	8.67E-8	

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METACORE KPA

WELCOME TO KEY PATHWAY ADVISOR

NEW ANALYSIS

1 File Upload
2 Analysis Settings
3 Run Analysis

20 loaded reports

KPA enables researchers to easily perform upstream and downstream analysis of gene expression – even if they have little to no bioinformatics experience.

KPA helps researchers generate key pathway maps with input genes and Key Hubs identified.

With its intuitive interface and powerful analytics, the Key Pathway Advisor can support a range of researchers for disease understanding and discovery.

DISCOVERY BIOLOGISTS
HELPING YOU TO:

- Easily submit your data and generate an automatic comprehensive analysis even if you have no bioinformatics experience

- Combine gene expression and gene variant data

- Get a better understanding of aberrant signal transduction using detailed pathway maps with differentially expressed genes and Key Hubs highlighted

- Learn the biology of the disease you are working on

TRANSLATIONAL RESEARCHERS
HELPING YOU TO:

- Connect experimental research and clinical studies for insights

- Study detailed candidate disease drivers, biomarkers, and target relations, as well as their effect on signal transduction pathways

BIOINFORMATICIANS
HELPING YOU TO:

- Provide advanced causal reasoning and synergy pathway analyses to identify possible disease-driving molecules and aberrant signal transduction pathways

- Analyze connections between expression, gene variant, and predicted Key Hubs using a detailed XLS report

- Share analysis results with biologist colleagues using a PDF report with pathway images and descriptions

PRE-CLINICAL SCIENTISTS
HELPING YOU TO:

- Find novel biomarker and drug target candidates

- Identify drug response molecular changes and their signal transduction effect

To learn more, visit lsresearch.thomsonreuters.com/pages/solutions/1/metacore