Key Pathway Advisor (KPA)

Key Pathway Advisor delivers a testable hypothesis in just three clicks

Who can benefit

- Discovery biologists, including those without bioinformatics experience

- Bioinformaticians

- Preclinical scientists

- Translational researchers

KPA highlights

- Find the biological meaning of your data with a drag-and-drop wizard

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

- Visualize how gene expression changes affect pathway activity (signaling pathway impact analysis)

- Align your data with current drug target and biomarker knowledge

Cortellis
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Clarivate Analytics

Comprehensive pathway analysis

High throughput analysis workflows (such as gene expression) are generally focused on identification of entities whose concentration differs between two conditions (case/control studies) and the biological pathways affected as a result. However, the observed molecular changes themselves may be a symptom/effect rather than the root cause of the condition under investigation.

Key Pathway Advisor (KPA) uses causal reasoning network analysis with your gene expression data to predict key hubs that may be transcriptional factors responsible for the observed expression changes. KPA leverages about 100,000 manually annotated high-quality protein/RNA/compound interactions (including more than 38,000 transcriptional regulation interactions) stored in its database to perform this analysis.

KPA also uses Signaling Pathway Impact Analysis (SPIA) to identify and visualize pathway activity changes caused by differential expression. In addition, it performs synergy pathway analysis to automatically define processes enriched with experimentally defined genes and predicted key hubs to highlight potential biologically relevant results.
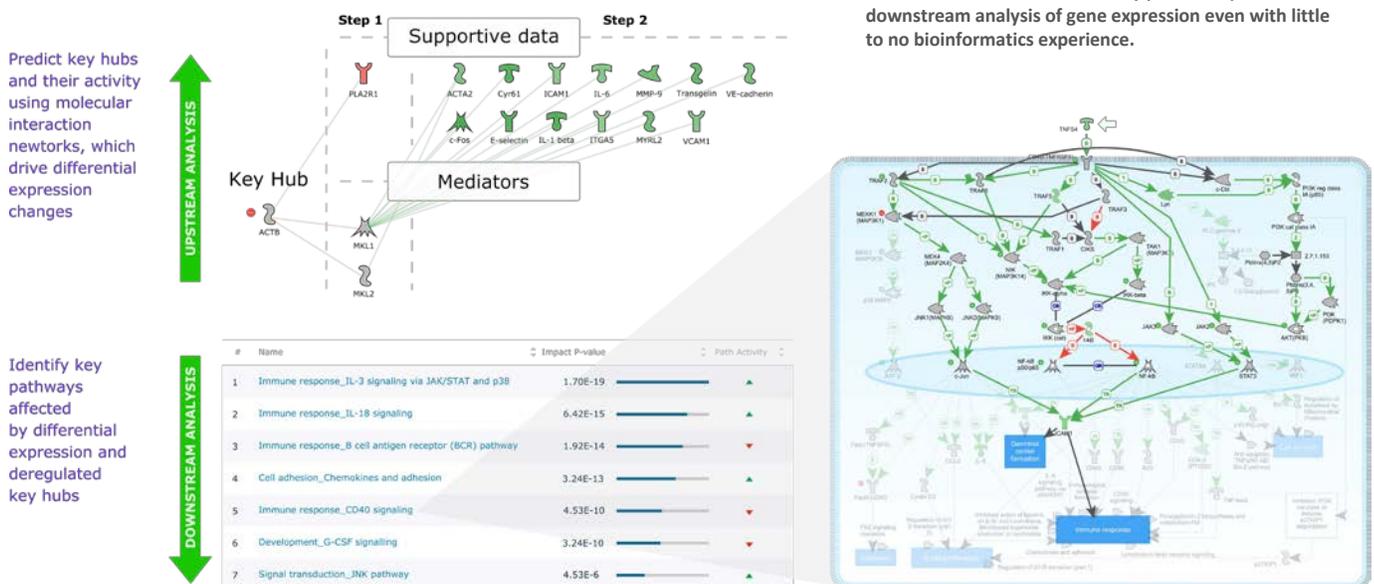
> *In just a few clicks, Key Pathway Advisor delivers the biological insight you need. No bioinformatics experience required.*

OMICs data analysis combined with prior knowledge

KPA enables faster, more intuitive analysis of gene expression and associated gene variant data. Like a biological version of the GPS in your car, KPA doesn't just visualize all possible targets, 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 also allows you to align your molecular changes with current knowledge on drug targets and putative biomarkers from *Clarivate's MetaBase* and *Integrity* databases – all in the same report as your analytical results. Combining these results allows you to see whether the observed changes have been seen before in your chosen condition or what clinical stage drugs targeting them in that condition have reached. Guided workflows in KPA make it easy to gain insight into your results in a straightforward, highly reproducible workflow.

KPA analysis approach

Predict key hubs and their activity using molecular interaction newtorks, which drive differential expression changes

UPSTREAM ANALYSIS

Identify key pathways affected by differential expression and deregulated key hubs

DOWNSTREAM ANALYSIS

#	Name	Impact P-value	Path Activity
1	Immune response_IL-3 signaling via JAK/STAT and p38	1.70E-19	▲
2	Immune response_IL-18 signaling	6.42E-15	▲
3	Immune response_B cell antigen receptor (BCR) pathway	1.92E-14	▼
4	Cell adhesion_Chemokines and adhesion	3.24E-13	▲
5	Immune response_CD40 signaling	4.53E-10	▼
6	Development_G-CSF signaling	3.24E-10	▼
7	Signal transduction_JNK pathway	4.53E-6	▲

KPA enables researchers to easily perform upstream and downstream analysis of gene expression even with little to no bioinformatics experience.

KPA supports a range of researchers for disease understanding and discovery

Discovery biologists

- Submit your data and generate an automatic comprehensive analysis, even with no bioinformatics experience.

- Combine gene expression and gene variant data

- Get a better visual understanding of aberrant signal transduction using detailed pathway maps with differentially expressed genes and key hubs highlighted.

- Use biomarker and drug target knowledge alignment to learn the biology of the disease you are working on.

Translational researchers

- Connect experimental research and clinical studies for insights.
- Study detailed candidate disease drivers, biomarkers, and target relations and their effect on signal transduction pathways.

Bioinformaticians

- Provide advanced causal reasoning and synergy pathway analyses to identify possible disease-driving molecules and aberrant signal transduction pathways.
- Analyze connections between expressions, gene variants, and predicted key hubs using a detailed XLS report.

Preclinical scientists

- Find novel biomarker and drug target candidates by automatically comparing your data with current.
- Identify drug response molecular changes and their signal transduction effect.

Key Pathway Advisor: a small investment with a potentially big return

Understanding the science behind your research has multiple commercial benefits. With *Clarivate Analytics* systems biology solutions, you maximize your chances for success and reduce your risk by using the best quality information available. Additionally, *Clarivate Analytics* systems biology solutions can provide an increase in scientific understanding and result in increased productivity, cost savings, and risk reduction.

Save time with more powerful analytics

"Something that I do with Clarivate in one afternoon would have taken a week before."
- Dr. Charles Lecellier, Principal Investigator, IGMM

"Within a couple of hours, we can now identify targets that we previously hadn't considered."
- A computational drug development team in a top five pharma company

"It would have taken up to a year previously to make a decision, but we have been able to make decisions now in a matter of months."
- A research scientist in a leading medical technology company

According to payscale.com, a research scientist earns an average salary of $76,601 per year. If that scientist takes one afternoon rather than a week to integrate and understand their data, and if this task is done weekly, this could provide potential annual savings of up to the equivalent salaries for 10 research scientists ($766,010).

Make the right decisions with high-quality data

Making fast decisions is not enough – they must also be the correct decisions. The average drug takes up to 14 years to reach full market approval[1] and there is increasing pressure on researchers to publish research early to secure further rounds of funding. If decisions are made on faulty data, it can result in a significant amount of wasted time, effort and money.

Content in *Clarivate Analytics* systems biology solutions is manually curated by scientists (PhD and MD-level). Independent studies have shown that the quality and completeness of the content in our solutions is significantly higher than any other solution studied—both commercial and public. In a 2011 study by Shmelkov et al. from the New York School of Medicine, *Clarivate* was found to have significantly higher levels of correct prediction of gold standard transcription factor targets when compared to other commercial and public databases (*Clarivate database* 84% vs. second place 36%).[2]

Increase your chances for clinical success

An increased knowledge of the biology of your target and disease has a significant positive effect on clinical success. Recently, AstraZeneca introduced their "five Rs" for success.[3] As part of the analysis, they found that 40% of clinical failures due to efficacy had no target disease linkage established and that 82% of projects with efficacy biomarkers succeeded. Their in-depth analysis of their pipeline successes and failures showed a clear correlation between an understanding of basic target and disease biology on project success:

 "Projects that showed greater confidence in target validation, genetic target linkage to disease, or a stronger understanding of the role of the target in the disease etiology were less likely to fail owing to lack of efficacy."[3]

Pfizer also found that 43% of their failures due to efficacy had not had their mechanisms sufficiently tested. Understanding the mechanisms and biology behind your research is a key indicator for success.[4] Good understanding appears to correlate with good chances of success. *Clarivate Analytics* systems biology solutions allow an increase in scientific understanding and facilitate a significant opportunity to increase productivity

Bibliography

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Who we are

Clarivate Analytics accelerates the pace of innovation by providing trusted insights and analytics to customers around the world, enabling them to discover, protect and commercialize new ideas faster. We own and operate a collection of leading subscription-based services focused on scientific and academic research, patent analytics and regulatory standards, pharmaceutical and biotech intelligence, trademark protection, domain brand protection and intellectual property management. *Clarivate Analytics* is now an independent company with over 4,000 employees, operating in more than 100 countries and owns well-known brands that include *Web of Science, Cortellis, Derwent, CompuMark, MarkMonitor* and *Techstreet*, among others.

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