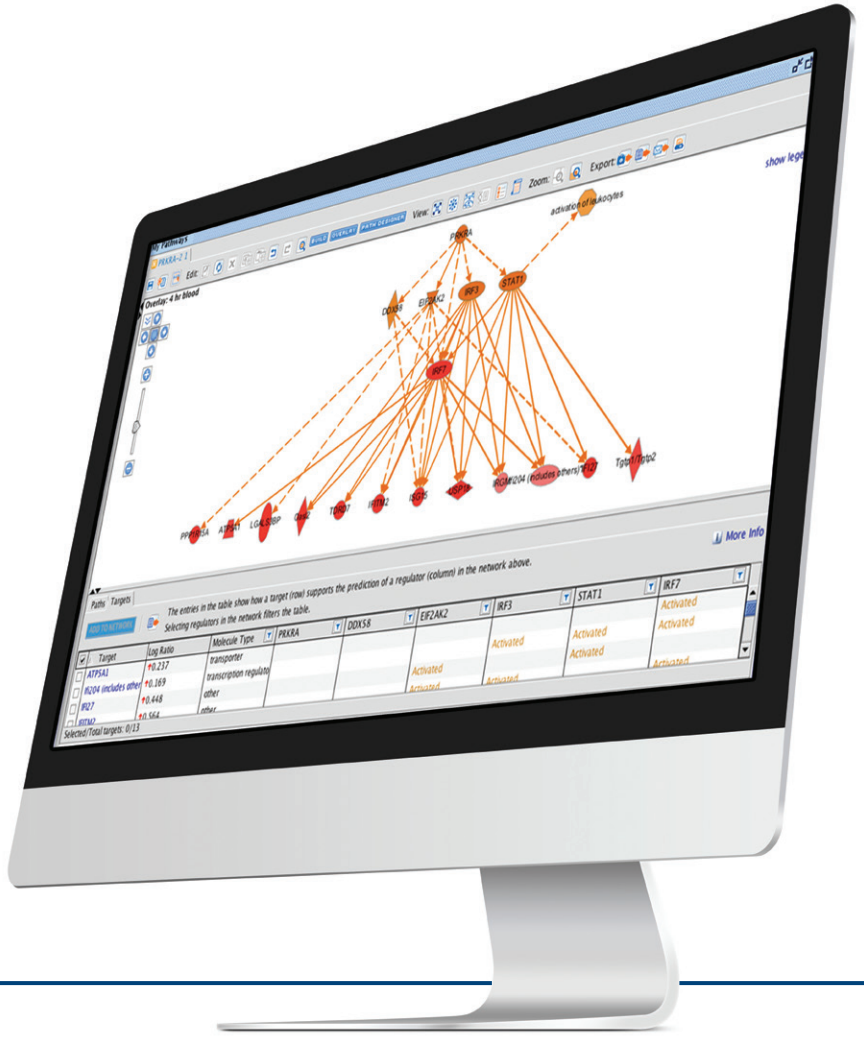
IPA® Advanced Analytics

Uncover causality — the next level of pathway analysis

Genomic, proteomic, metabolomic and other life science data are puzzle pieces to complex biological networks and pathways. Leveraging the unique structure and unparalleled content of the QIAGEN® Knowledge Base and Ingenuity® Pathway Analysis (IPA) reveals significant molecules, biological pathways and networks underlying complex 'omics data. Now, IPA Advanced Analytics expands the scope, empowering you to discover novel mechanisms of action.



Sample to Insight

Pathway, network and functional analysis with IPA

IPA is a web-based software application for the analysis, integration and interpretation of data derived from gene expression experiments including RNA-seq, microRNA and SNP microarrays, metabolomics, proteomics and small-scale experiments that generate gene and chemical lists. Downstream Effects Analysis predicts cellular functions, disease processes and other phenotypes impacted by patterns in an analyzed dataset. Upstream Regulator Analysis identifies regulators (transcription factors, cytokines, kinases, etc.) directly linked to the targets in analyzed data and whose activation or inhibition may account for observed changes.

IPA Advanced Analytics — get the most out of your data

Causal Network Analysis and BioProfiler capabilities of IPA Advanced Analytics identify plausible causes for changes observed in an analyzed dataset.

The innovative features of IPA Advanced Analytics:

- Generate novel hypotheses for mechanisms of action or drug targets
- Prioritize predicted regulatory networks by their connections to diseases or phenotypes of interest
- Uncover causal relationships relevant to your experimental data

Generate informed hypotheses about causality

The Causal Network Analysis feature of IPA Advanced Analytics uses powerful algorithms to generate multi-leveled regulatory networks that may explain the gene expression changes exhibited in a dataset. The core Upstream Regulator Analysis of IPA identifies upstream molecules that are directly connected to the targets exhibiting changes in a dataset. So, for example, in a study on gene expression changes in blood of mice exposed to toxic welding fumes, IPA identified activation of transcription factor IRF7 as a causal mechanism for the observed upregulation of targets in the analyzed dataset.

Causal Network Analysis goes the next step. It enables the discovery of novel regulatory mechanisms by expanding upstream analysis to include regulators that are not directly connected to targets in the dataset. Thus, in our previous example, IRF7 may be an intervening molecule of the regulatory activity of protein kinase PRKRA (depicted as the root of the causal network in Figure 1). The user can quickly visualize the regulatory networks most closely associated with a particular disease or phenotype and then prioritize the most interesting and relevant causal networks as hypotheses to explain patterns in the dataset. Furthermore, by prioritizing resulting networks by molecule, disease, function or phenotype, the user can discover more distant connections between the causal network and the research or therapeutic area of interest.

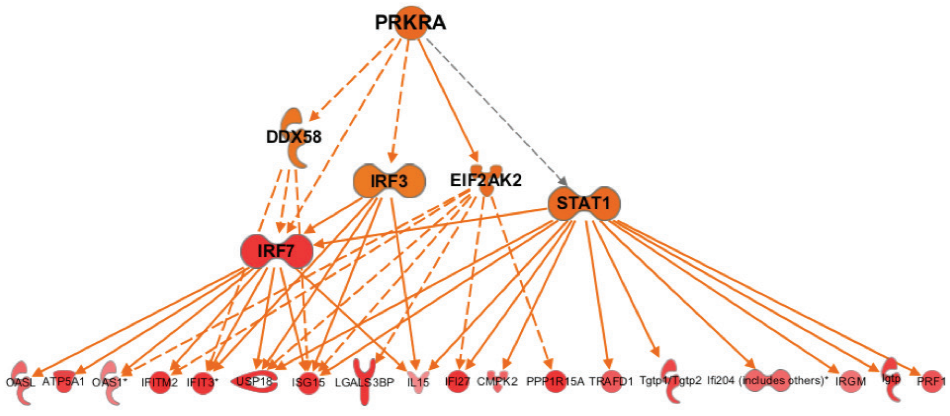


Figure 1. Causal Network Analysis identifies multi-tiered regulatory networks underlying patterns in data. Gene expression data from blood of mice exposed to welding fumes were analyzed for upstream regulators. Standard analysis identified the interferon regulatory factor IRF7. Causal Network Analysis expanded the scope to include more regulators and identified the protein kinase PRKRA as a possible regulatory node, which may work through IRF7 to elicit the observed expression changes.

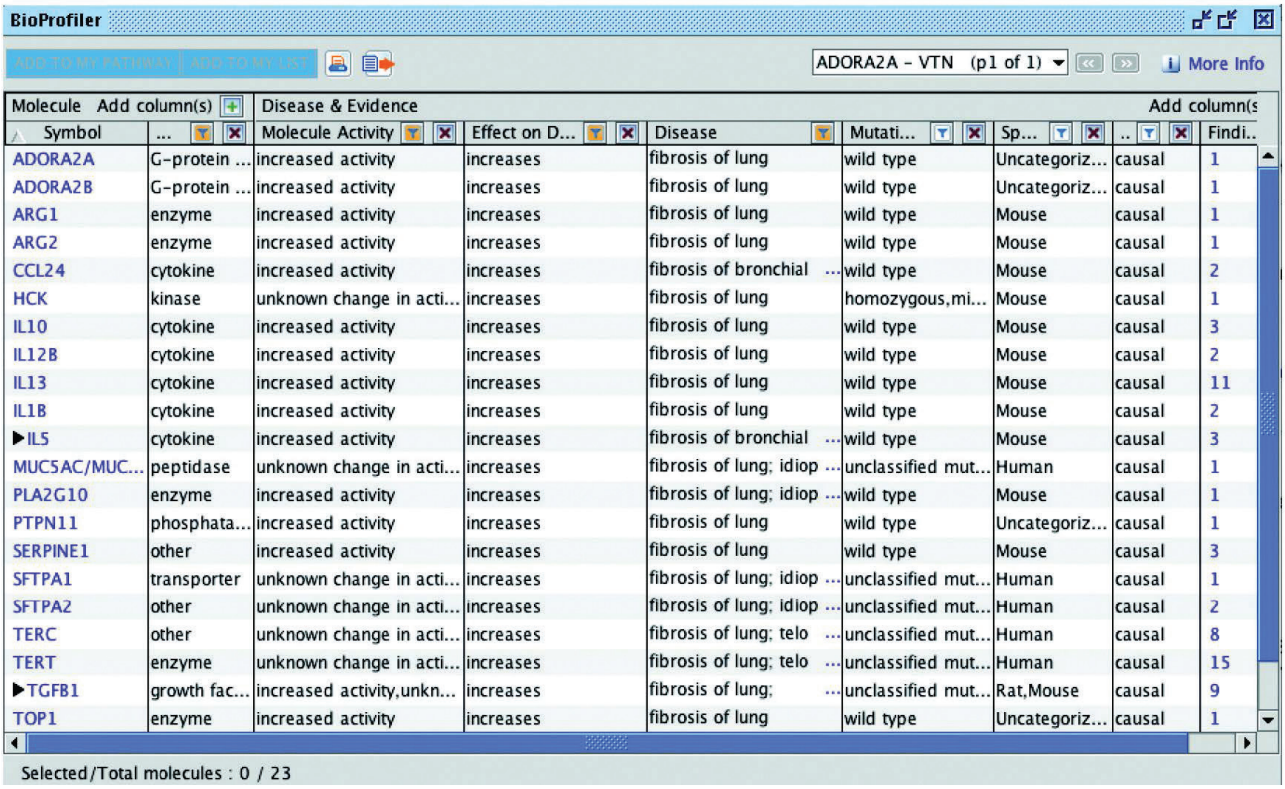


Figure 2. Comprehensive profiles of phenotypes in BioProfiler. Capitalizing on the highly interconnected content of the QIAGEN Knowledge Base, BioProfiler delivers detailed listings of genes and compounds implicated in diseases and other phenotypes, which the user can filter and sort to hone in on interesting causal mechanisms.

Identify causally relevant molecules and genes

The QIAGEN Knowledge Base contains over 6 million facts extracted from scientific publications and databases and structured so that each relationship between molecule, diseases and phenotype is characterized and searchable. BioProfiler probes this repository of scientific information to generate molecular profiles of diseases, phenotypes and biological processes (e.g., apoptosis) listing all the genes and compounds that have been associated with the profiled term. The power of this tool lies in the intuitive and comprehensive layout of the results (Figure 2) enabling the user to find, filter and prioritize genes and compounds based on the research question at hand. The user can focus on molecules of interest, find causally relevant genes, filter for specific genetic evidence or for species and explore associations with similar diseases or phenotypes. The surfaced data can then be examined further in the context of pathways using all available IPA features.

Relationship Export

The Relationship Export capability in IPA enables you to export relationships from networks and pathways for further visualization.

You can export the structural information contained within IPA networks or pathways for visualization in other tools such as Cytoscape. The export format contains relationships modeled as triples: Node A -> Relationship -> Node B.

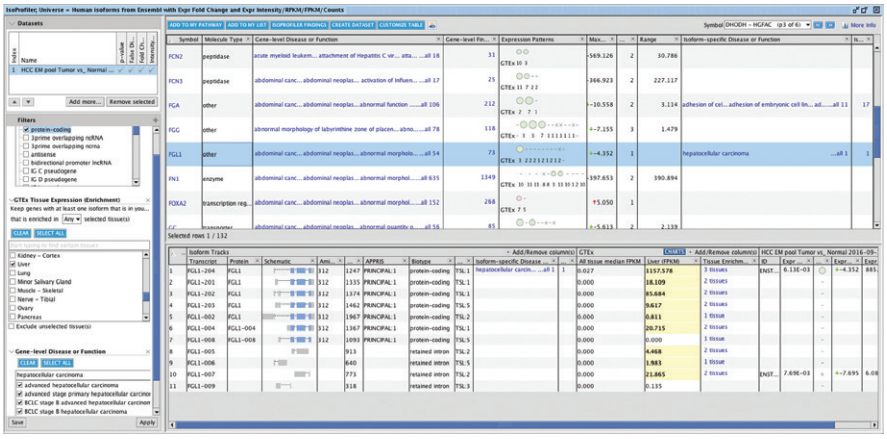


Figure 3: Prioritizing splice variants (isoforms) with IsoProfiler. Filter your transcriptomics datasets to focus on transcripts with biological relevance to your experiment, for example those expressed in certain tissues or with findings pertaining to a certain disease.

Phosphorylation Analysis

Changes in the phosphorylation states of proteins provide an important regulatory mechanism in mammalian cells. Discover upstream regulators and causal network master regulators that may be driving the changes in phosphorylation levels of the proteins in your phosphoproteomics dataset. Visualize how the phosphorylated proteins affect Canonical Signaling pathways. These results provide testable hypotheses by identifying potential signaling cascades from the phosphorylation patterns in your dataset.

RNA-seq support with Isoform View and IsoProfiler

IsoProfiler helps you determine which isoforms from your RNA-seq datasets have interesting biological properties relevant to your research project. For example, genes where isoforms are both upregulated and down regulated in the same dataset, which may have important functional consequences. Find cases of isoform switching – when the most highly expressed (highest RPKM) isoform for a gene differs between the experiment and the control samples, find tissue-specific isoform expression with integrated GTEx data or explore all the cases where a gene expresses multiple protein-coding isoforms or are known to impact a disease or function.

Maximize insights into your data

With supporting evidence from published data and powerful analytics, IPA Advanced Analytics enables you to generate testable hypotheses and validation experiments for the causal connections embedded in your data. IPA Advanced Analytics takes you beyond standard analyses so you can focus on novel insights about the causes of disease or other phenotypes of interest.

Get the most out of your biological analysis.
Visit **qiagenbioinformatics.com/products/ingenuity-pathway-analysis/**

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