

Applications

- Target Identification and Validation
- Biomarker Discovery
- Drug Mechanism of Action
- Drug Mechanism of Toxicity
- Disease Mechanisms

Experimental platforms supported

- Gene Expression
- Proteomics
- Genotyping
- Metabolomics
- siRNA
- miRNA **new**

Identifiers supported in IPA

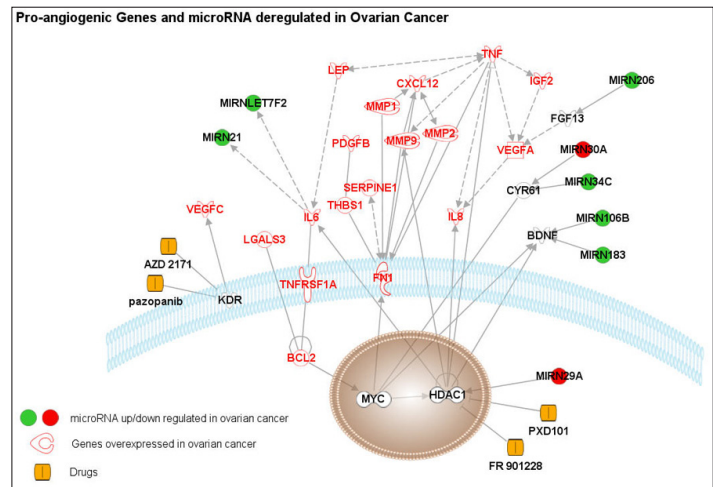
- Affymetrix (Exon/Gene Expression, 3' IVT Expression)
- Affymetrix SNP ID (Genotyping)
- Agilent (Gene Expression, microRNA) **new**
- Applied Biosystems
- CAS Registry
- CodeLink
- dbSNP IDs (including Illumina genotyping arrays with dbSNP ids) **new**
- Entrez Gene
- GenBank
- GenPept
- GI Number
- HUGO Gene Symbol
- Illumina (whole-genome arrays, microRNA arrays)
- International Protein Index
- KEGG ID
- miRBase (mature) **new**
- PubChem CID
- RefSeq
- UniGene
- UniProt/SwissProt Accession

Species supported in IPA

- Human
- Mouse
- Rat
- Canine
- Additional species supported via ortholog mapping

Ingenuity Pathways Analysis 7.5

IPA™ is an all-in-one, web-based application that enables you to analyze, integrate, and understand data derived from gene expression, microRNA, and SNP microarrays; metabolomics and proteomics experiments; and small-scale experiments that generate gene lists. With IPA you can search for targeted information on genes, proteins, chemicals, and drugs, and build interactive models of your experimental systems. IPA's data analysis and search capabilities help you understand the significance of your data, specific target, or candidate biomarker in the context of larger biological or chemical systems, backed by the Ingenuity knowledge base of highly structured, detail-rich biological and chemical findings.



Path Designer transforms networks and pathways into publication quality representations of biological systems.

Search & Exploration of Biological and Chemical Knowledge

IPA's Search and Explore allows researchers to generate targeted search results, and act on those results to create biological models representing their experimental systems.

My Pathways: For building custom pathway and gene list libraries

Start with gene lists from IPA search results, an existing IPA Network or Canonical Pathway, or an uploaded list of targets or biomarkers. Then use the Build tools to identify upstream activators and inhibitors or downstream targets of those genes, layer in additional biological information or experimental data, and build event-specific pathways such as:

- microRNA-mRNA target networks **new**
- Transcriptional networks
- Phosphorylation cascades
- Protein-Protein or Protein-Promoter Interaction Networks
- Chemical/Drug effects on proteins

Use Context Filters to: **new**

- Focus your pathways on genes implicated in a disease, or detected in a specific cell line, cell or tissue

- Narrow in on regulatory events that were demonstrated in a particular cellular context
- Use the Path Explorer tool to:
- Find relevant regulatory paths and physical interactions between genes of interest
 - Identify shortest literature-supported paths between drugs or genes associated with a disease or toxicity phenotype

Path Designer: The easy-to-use pathway design and publishing tool

Transform your networks and pathways in IPA into publication-quality pathway graphics rich with color, customized text and fonts, species-specific nomenclature, biological icons, organelles, and custom backgrounds. Path Designer pathways are fully interactive and supported by the high quality content stored in IPA. This easy to use graphics package ensures that your entire workflow – from data analysis to publication and communication of insights to colleagues – can be completed within IPA.

Detail-rich, highly structured knowledge for over

- 16,900 human, 12,150 mouse, and 7,100 rat genes
- 7,580 chemicals
- ~962,000 biological and chemical concepts
- ~2.35 million literature referenced findings
- ~921,000 synonyms, ~2.4 million synonym-concept pairs

Additional sources of content, relationships in IPA

- Entrez Gene
- RefSeq
- OMIM
- GWAS Database new
- Gene Ontology
- Tissue Expression Body Atlas
- NCI-60 Cell Line Expression Atlas
- KEGG metabolic pathway information
- LIGAND enzyme/substrate reactions
- BIND, DIP, MINT, MIPS, BIOGRID, INTACT, COGNIA protein-protein interactions (updated) new
- ARGONAUTE 2, TARBASE microRNA-mRNA targeting interactions

Technical Requirements

Operating System

Vista, Windows XP SP2 and Macintosh 10.4.11, 10.5.2

Web Browser

Internet Explorer 6.0 or higher.
Firefox 1.5 or higher is recommended.
For Mac OS, Safari 3.1

Memory

Minimum of 512MB RAM (1GB RAM recommended).

Java Runtime Environment

Version 1.5 or higher.

Deployment

IPA can be accessed as a web hosted or a deployed solution.

Gene & Chemical Search: Generate and compare targeted lists of genes, druggable proteins, and chemicals

- Identify all GPCRs known to play a role in obesity.
- Find all genes implicated in angiogenesis, understand which signaling pathways they participate in, and which are targeted by candidate compounds.
- Identify all compounds (FDA-approved and clinical candidates) that target prostate cancer genes, or pro-metastatic genes.
- Use the Compare feature to identify genes and chemicals that participate in angiogenesis, for example, but not in metastasis.

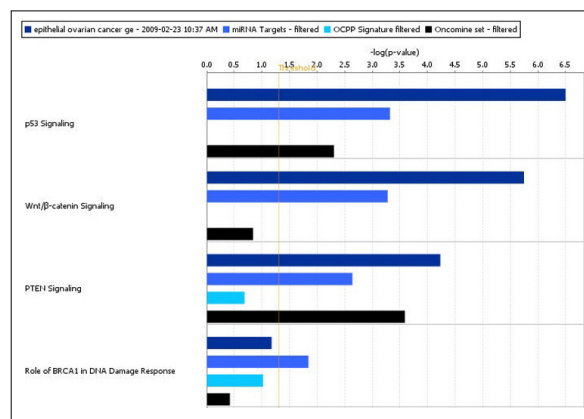
Data Analysis & Interpretation



IPA's Data Analysis and Interpretation unlocks the insights buried in experimental data by quickly identifying relationships, mechanisms, functions, and pathways of relevance, allowing researchers to move beyond statistical analysis to novel biological insights and better experimental design.

IPA Core Analysis delivers a rapid assessment of the signaling and metabolic pathways, molecular networks, and biological processes that are most significantly perturbed in a dataset of interest.

- Understand the relative impact of changes in mRNA, microRNA, protein or metabolite levels in the context of well-characterized pathways. new
- Identify the cellular and disease phenotypes most significant to a set of genes, and understand how those genes impact that phenotype, i.e. whether they increase or decrease a biological process.
- Choose various statistical methods for narrowing in on the most significant gene to function relationships, including the Benjamini-Hochberg method of accounting for multiple testing.
- Find results and information most relevant to you: construct networks of interaction and regulatory events focused on your genes and proteins of interest, or narrow in on analysis results most closely aligned with your experimental model.
- Compare affected pathways and phenotypes across platform, time, dose, or patient population. new



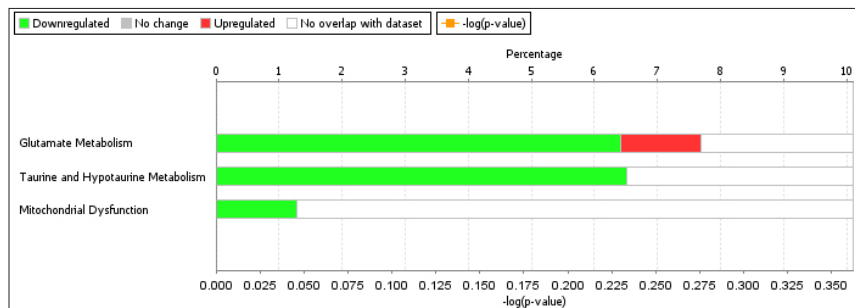
Identify pathways implicated by multiple experimental platforms

IPA-Metabolomics™ overcomes the metabolomics data analysis challenge by providing the critical context necessary to gain biological insight into cell physiology and metabolism from metabolite data.

- Analyze metabolomics data (lists of CAS, PubChem CID, KEGG identifiers) in the context of dynamic metabolic and signaling pathways.
- Understand which biological processes and phenotypes your metabolites are involved in.
- Search and explore Ingenuity's extensive repository of chemical knowledge to understand what affects metabolite synthesis and what that metabolite regulates.
- Integrate mRNA, microRNA, SNP, proteomics, and metabolomics data for a complete systems biology approach to biomarker discovery, molecular toxicology, and understanding drug mechanism of action and toxicity.

IPA-Tox™ delivers a focused toxicity and safety assessment of candidate compounds, and provides a more complete understanding of pharmacological response, drug mechanism of action, and mechanism of toxicity.

- Determine whether compound-induced changes in transcript or protein levels are significantly associated with Toxicity Lists - functional gene groupings based on critical biological processes and key toxicological responses. These lists describe adaptive, defensive, or reparative responses to xenobiotic insult and can be used to understand biological responses in liver, kidney, or heart.
- Understand the relationship between transcript, protein, or metabolite changes and Toxicity Functional Categories, which cover a wide spectrum of well-known drug related injuries and pathologies useful for the drug discovery and development process.
- Integrate Toxicity Functional Analysis results with Toxicity Lists Analysis insights to link experimental data to clinical pathology endpoints and support mechanistic hypothesis generation.



Understand biological response to drug treatment.

IPA-Biomarker™ identifies the most promising and relevant biomarker candidates within experimental datasets.

- The Biomarker Filter capability rapidly prioritizes biomarker candidates based on biological characteristics most relevant to a discovery study:
 - Determine if proteins are detected in bodily fluids including blood, bronchoalveolar lavage fluid, CSF, PBMCs, saliva, sputum, synovial fluid, tears, and urine.
- Filter by expression patterns in over 30 normal tissues as well as the NCI-60 panel of cell lines.
- Identify candidate biomarkers implicated in disease processes
- The Biomarker Comparison feature generates lists of candidate markers that are unique to one treatment or patient sample, or common across all treatments and patients.

Select filters that are most relevant to your biomarker discovery project. An "OR" operation is executed within each filter and an "AND" operation across the filters.

Species ?

Tissues & Cell Lines ?

Biofluids Cerebral Spinal Fluid... ?

Diseases ?

- Select all
- Blood
- Bronchoalveolar Lavage Fluid
- Cerebral Spinal Fluid
- PBMC Cells
- Plasma/Serum
- Saliva
- Sputum
- Synovium/Synovial Fluid
- Tears
- Urine

Filter Summary

Consider only molecules where fluids = Cerebral Spinal Fluid OR Plasma/Serum

Narrow in on the biomarker candidates in your dataset that meet multiple biological criteria.

Content





IPA's knowledge base is the largest of its kind and features the most descriptive and detailed structure, the highest degree of accuracy, and the largest number of literature findings. It provides researchers with a tremendous resource for searching relevant and substantiated knowledge from the literature, and for interpreting experimental results in the context of larger biological systems for greater confidence with research decisions.

Biological and Chemical Information

IPA's expert-extracted content includes modeled relationships between chemicals, proteins, genes, complexes, cells, cellular components, tissues, drugs, cellular processes, diseases, and clinical phenotypes. Gain access to:

- Gene View pages with comprehensive, species-specific knowledge about gene function and regulation, tissue expression patterns, subcellular location, mutations, and disease associations tissues as well as the NCI-60 panel of cell lines

Biological and Chemical Information (continued)

- Chem View pages with chemical and pharmacological information on clinical candidates and FDA approved drugs, known targets, effects on gene expression and protein activity, drug metabolism, and drug protein adducts
- Compound toxicity and ADME information on lethal dose, inhibitory concentration, pharmacokinetic properties, AUC, clearance, and CYP regulation
- Drug and chemical information such as drug manufacturer, clinical trial sponsor, and link to NCT website for each trial displayed
- Knowledge of genes, proteins, and compounds associated with thousands of diseases, including over 18,500 gene to disease associations involving 16,000 distinct SNPs 
- Tissue and Cell Line Expression Atlases containing positive gene expression calls for over 30 normal tissues and the NCI-60 panel of cell lines
- Experimentally demonstrated and predicted mRNA targets help you understand the impact of microRNA deregulation
- Thematically grouped libraries of well characterized signaling and metabolic pathways, including 

a significant number of new disease pathways for cancer, metabolic disorders and immune disorders.

- Millions of molecular interactions and regulatory events extracted from the scientific literature
- Semantic and linguistic consistency based on Ingenuity's comprehensive ontology
- Synonym and homonym mapping to ensure correct object identity

Manually Curated Information

All of the knowledge in IPA is manually curated and modeled from primary literature sources, including peer-reviewed journal articles, review articles, and textbooks, by a team of Ph.D. scientists, ensuring that customers have access to relevant findings that are supported by experimental evidence.

Unparalleled Structure and Contextual Details

The content in IPA contains the level of contextual detail required to understand the complexity of biological and chemical relationships, including: species specificity, cell type context, mutations, post-translational modifications sites, epigenetic modifications, and experimental methods used. This level of detail ensures that researchers can access knowledge and generate hypotheses relevant to their experimental system.

Frequent Updates

The content in IPA is updated regularly to provide customers with high-impact knowledge on a timely basis.

Discover the power of Ingenuity Pathways Analysis.

Register for a complimentary and fully functional trial at www.ingenuity.com/trial

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About Ingenuity

Ingenuity Systems is a leading provider of information solutions for the exploration, interpretation, and analysis of life science information. Ingenuity's products and services have one common goal — to help life science researchers generate maximum value from all types of biological and chemical knowledge. Ingenuity offers a broad range of flexible solutions that can be tailored to the needs of its clients, including academic and therapeutic area researchers, computational biologists and informatics departments, and suppliers in the life sciences industry. All Ingenuity products leverage the Ingenuity knowledge base, the largest database of its kind, which houses biological and chemical relationships extracted from the scientific literature. Today, Ingenuity's solutions are used by thousands of researchers at hundreds of leading pharmaceutical, biotechnology, and academic research institutions worldwide. Ingenuity was founded in 1998 and is headquartered in Redwood City, California with offices in Massachusetts, the United Kingdom, Japan, and France.