

Applications

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

Experimental platforms supported

- Gene Expression (mRNA, miRNA, microarray, next-gen sequencing, qPCR) new
- Proteomics
- Genotyping
- Metabolomics

Identifiers supported in IPA

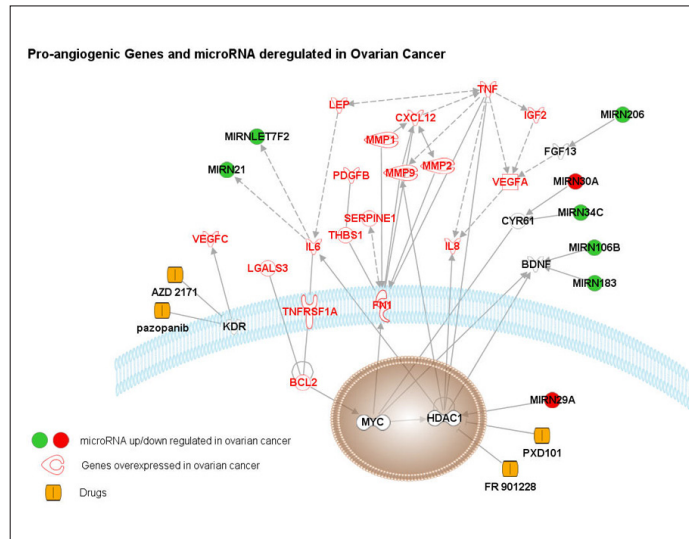
- Affymetrix (Exon/Gene Expression, 3' IVT Expression)
- Affymetrix SNP ID (Genotyping)
- Agilent (Gene Expression, microRNA)
- Applied Biosystems (Gene Expression, microRNA)
- CAS Registry
- CodeLink
- dbSNP IDs (including Illumina genotyping arrays with dbSNP ids)
- Entrez Gene
- GenBank
- GenPept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

Species-specific identifiers supported in IPA

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

IPA™ 8.0

IPA™ is an all-in-one, web-based software 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



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

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.

Search & Exploration of Biological and Chemical Knowledge



IPA's Search and Explore allows you to generate targeted search results, and act on those results to create biological models representing your 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
- Protein-Protein or Protein-Promoter Interaction Networks
- Transcriptional networks
- Phosphorylation cascades
- Chemical/Drug effects on proteins

Use Context Filters to:

- Highlight the relationships published within a particular date range. new
- Identify clinical biomarkers in a Network or My Pathway. new
- 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.

Detail-rich, highly structured knowledge for over new

- 17,000 human, 12,400 mouse, and 7,200 rat genes
- 11,200 chemicals
- 1,036,000 biological and chemical concepts
- 2.49 million literature referenced Findings
- 1 million synonyms, ~2.53 million synonym-concept pairs

Additional sources of content in IPA

- Entrez Gene
- RefSeq
- OMIM
- GWAS Database
- Gene Ontology
- Human Metabolome Database (HMDB)
- GNF 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)
- ARGONAUTE 2, TARBASE microRNA-mRNA targeting interactions
- Clinicaltrials.gov
- Drugs@FDA
- Mosby's Drug Consult
- Goodman & Gilman's' Pharmacological Basis of Therapeutics
- DrugBank

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 1.5.0_06 and 1.6.0_15 (Vista and Windows XP SP2); 1.5.0_13, 1.5.0_16, and 1.6.0_05 (Mac 10.4.11, 10.5.2)

Deployment

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

Gene, Chemical, & Pathway Search: Generate and compare targeted lists of genes, druggable proteins, biomarkers, 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.
- Quickly identify the subset of disease genes that are used as biomarkers in various clinical applications. new

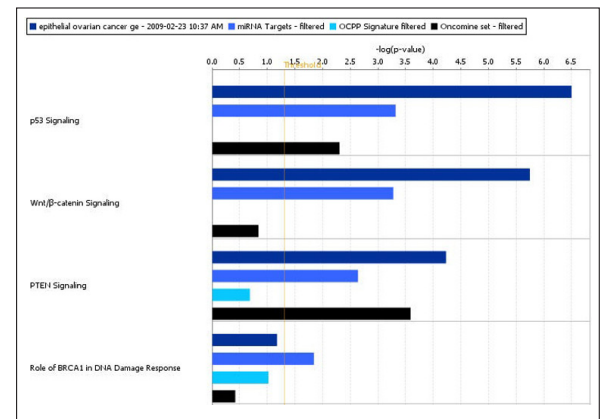
Data Analysis & Interpretation



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

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.
- 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.
- Optimize visualization and biological context of analyses with Context and new Network Size parameters.
- 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.



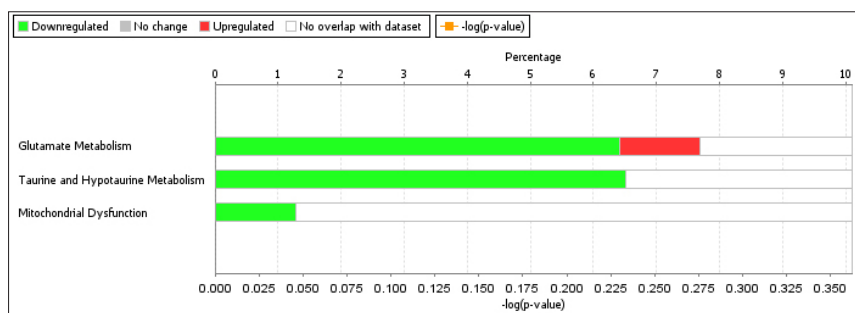
Identify pathways implicated by multiple experimental platforms

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 and what regulates their synthesis, as well as the metabolite subcellular location and detection in biofluids.
- Integrate mRNA, microRNA, SNP, proteomics, and metabolomics data for a complete systems biology approach to understanding disease, biomarker discovery, molecular toxicology, and understanding drug mechanism of action.

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. These lists describe adaptive, defensive, or reparative responses to xenobiotic insult and can be used to understand biological responses in liver, kidney, or heart.
- Identify genes, proteins, metabolites that are used in the clinic as biomarkers of drug safety. **new**
- 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.
- Integrate Toxicity Functional Analysis results with Toxicity Lists Analysis insights to link experimental data to clinical pathology endpoints and support mechanistic hypothesis generation.



Understand molecular 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:
 - Identify proteins that are being used in the clinic as biomarkers of disease diagnosis and prognosis, disease progression, markers of drug efficacy and safety, and patient response to therapy. **new**
 - Determine if proteins are detected in over 10 bodily fluids including blood, bronchoalveolar lavage fluid, CSF, PBMCs, saliva, and urine.
 - Filter by expression patterns in 30 normal tissues as well as the NCI-60 panel of cell lines and over 30 primary immune cell types and cell lines. **new**
- 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.

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

Communication & Collaboration Tools



IPA's Sharing and Reporting features enable you to clearly communicate biological insights from analyses. You can build interactive, publication-quality pathways and graphics that articulate key molecular mechanisms, and share datasets and analyses to facilitate collaborations.

Dynamic Pathway and List Reports: *Helpful summaries of most relevant biological information* new

Understand the broader biological and therapeutic relevance of a particular pathway or gene list by generating reports with detailed summaries and tables including pathway descriptions, top three related biological processes, drugs that target pathway members, and targets in the pathway.

- Generate custom reports for any My Pathway or My List in IPA including customer uploaded lists, and gene or chemical lists generated from IPA searches for diseases, processes.

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.

Share Module: *Tools to facilitate collaboration*

Create a shared folder containing all relevant datasets, analyses, pathways, and lists that are relevant to a given project. Share that project with colleagues, project team members to facilitate iteration, hypothesis generation, and design of validation studies.

Content



IPA is unique because it leverages the Ingenuity Knowledge Base, a database of manually curated and structured biological and chemical relationships called Findings. It provides you 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 Findings include modeled relationships between chemicals, proteins, genes, complexes, cells, cellular components, tissues, drugs, cellular processes, diseases, and clinical phenotypes. In IPA, you can access:

- Gene View pages with comprehensive, species-specific knowledge about gene function and regulation, tissue expression patterns, subcellular location, mutations, and disease associations
- 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, and 1,200 clinical biomarkers associated with over 190 diseases new
- Tissue and Cell Line Expression Atlases containing positive gene expression calls for 30 normal tissues, the NCI-60 panel of cell lines, and over 30 primary immune cell types and cell lines

Biological and Chemical Information (continued)

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

Manually Curated Information

The vast majority of Findings in the Ingenuity Knowledge Base are 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 you have access to relevant Findings that are supported by experimental evidence.

Unparalleled Structure and Contextual Details

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

Frequent Updates

The Findings in IPA are updated regularly to provide you with high impact knowledge on a timely basis. Findings that populate Gene Views, Chem Views, and Molecular Networks are updated weekly. Full content releases to IPA are provided quarterly.

Discover the power of Ingenuity Pathways Analysis.

Register for a complimentary and full functional trial at:

<http://www.ingenuity.com/trial/start.html>

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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 Switzerland, France, the United Kingdom, Japan, and Singapore.