IPA® 9.0

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, proteomics, and RNA-Seq experiments; and small-scale experiments that generate gene and chemical 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.

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

Experimental approaches supported
- RNA-Seq
- microarray
- microRNA
- mRNA
- qPCR
- proteomics
- genotyping
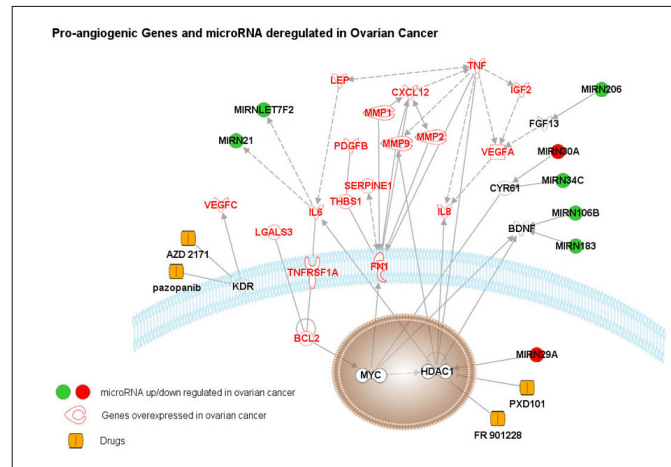
Identifiers supported in IPA
- Affymetrix (Exon/Gene Expression, 3' IVT Expression)
- Affymetrix SNP ID (Genotyping)
- Agilent (Gene Expression, microRNA)
- Applied Biosystems (Gene Expression, microRNA)
- CAS Registry
- CodeLink
- dbSNP IDs (including Illumina genotyping arrays with dbSNP ids)
- Entrez Gene
- Ensembl (new)
- GenBank
- GenPept
- GI Number
- HUGO Gene Symbol
- Human Metabolome Database (HMDB)
- Illumina (whole-genome & microRNA arrays)
- International Protein Index
- KEGG ID
- miRBase (mature)
- PubChem CID
- RefSeq (new)
- UCSC Human Isoform IDs (hg 18 & hg 19)
- UniGene
- UniProt/SwissProt Accession

Species-specific identifiers supported in IPA
- Human
- Mouse
- Rat
- Canine
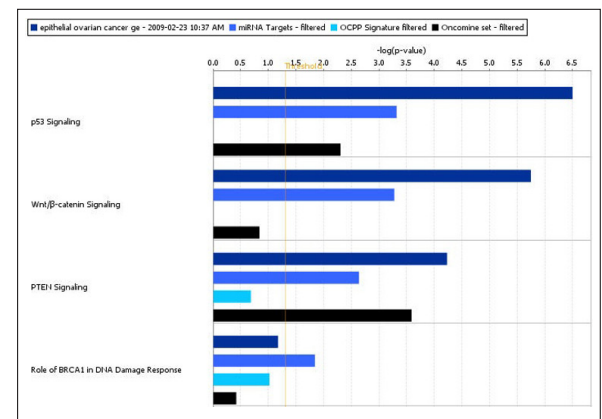- Additional species supported via ortholog mapping

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.

Identify pathways implicated by multiple experimental platforms.

- Optimize visualization and biological context of analyses with Context and 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.

- Interpret RNA-Seq data in the context of known biology to quickly narrow in on what is most valuable in your dataset.

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 HMDB, 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.

- 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.
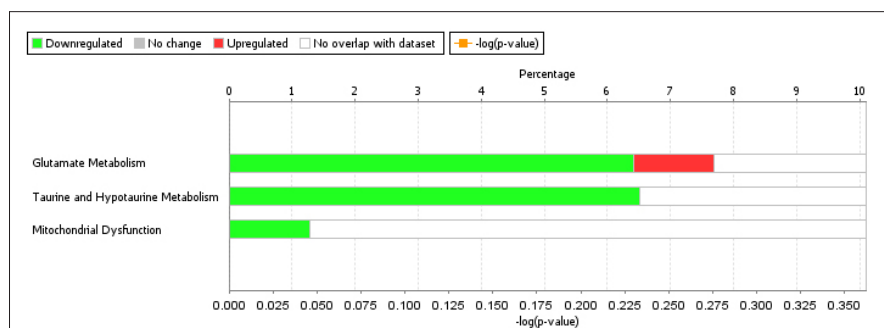
Understand molecular response to drug treatment.

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 genes, mRNA, proteins and metabolites 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.• 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.

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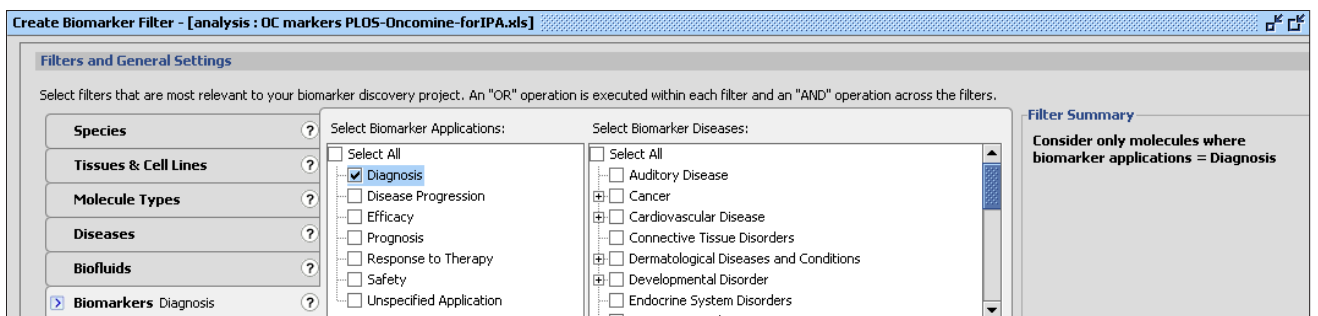
Narrow in on the biomarker candidates in your dataset that meet multiple biological criteria.

MicroRNA Target Filter combines filtering tools and microRNA-mRNA content to provide insight into the biological effects of microRNAs. *new*

• Identify mRNA targets for microRNAs using predicted microRNA –mRNA binding relationships from TargetScan, plus experimentally validated relationships from TarBase.

• Reduce number of steps to confidently identify targets by examining microRNA-mRNA pairings, exploring the related biological context of these relationships, and filtering mRNA targets based on relevant biological characteristics, all within a single tool.

• Easily prioritize mRNA target interactions based on confidence level of interaction predictions, source, or role/presence is species, diseases, tissues, pathways, cell lines, molecular types, and more.
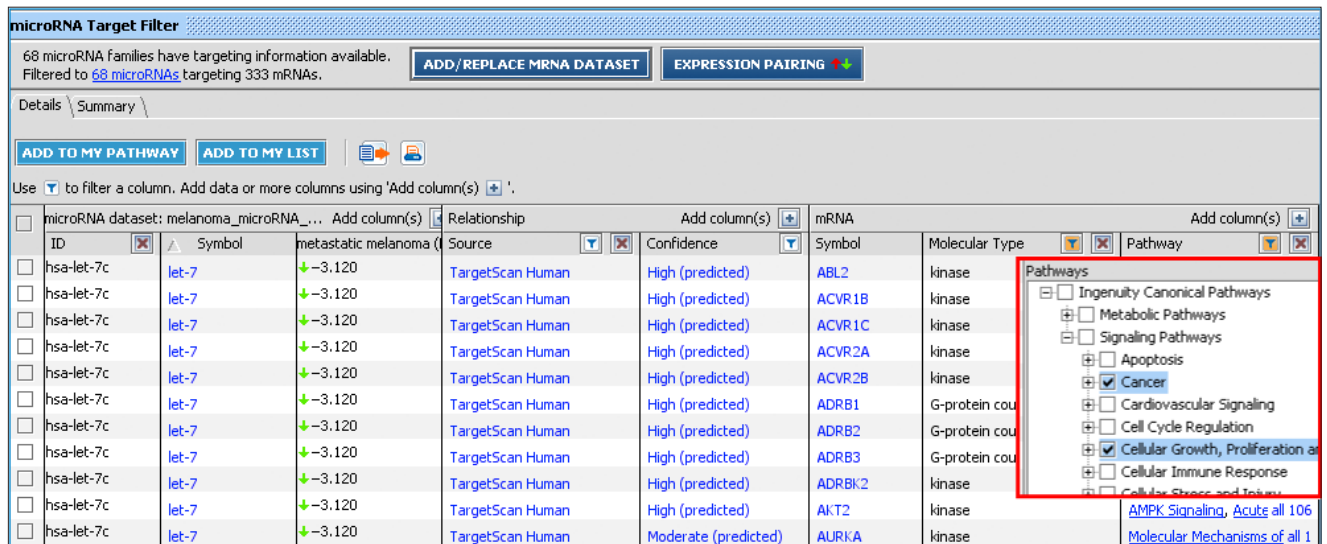
Filter and prioritize microRNA target relationships based on the biological context most relevant to your experiment (species, disease, pathway, tissue, cell line, molecular type, etc). Here, we filter on pathway.

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 or chemical 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
- Transcriptional networks
- Phosphorylation cascades
- Protein-protein or protein-promoter interaction networks
- Chemical/Drug effects on proteins

IPA Reagent View[beta]:
- Easily locate reagents information for genes and proteins in your experimental system, and link to vendor websites for more information or to place an order.
- Quickly design validation experiments to test hypotheses within specific experimental parameters.

Context Filters:
- Highlight the relationships published within a particular date range.
- Identify clinical biomarkers in a Network or My Pathway.
- Narrow in on regulatory events that were demonstrated in a particular cellular context.

Path Explorer tool:
- 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.

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.

Communication & Collaboration Tools

IPA provides a central place to analyze molecular data, generate testable hypotheses, and build and visualize molecular models of experimental systems. Update models with recent insights and generate custom, interactive reports to communicate and share insights with colleagues.

Professional Dynamic Reports: *Helpful summaries of relevant information.*
Understand the broader biological and therapeutic relevance of a particular pathway, gene or molecule list (including uploaded proprietary lists), or analysis result by generating reports with detailed summaries and tables including pathway descriptions, top related biological processes, drugs that target pathway members, and targets in the pathway. These dynamic reports enable faster decision making and hypothesis generation, allow for accurate versioning, and can be saved and exported as a fully interactive PDFs, so you can easily share insights and link back to the underlying knowledge in IPA.

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. You can also send colleagues professional

pathway reports with links to Path Designer pathways. Path Designer lets you complete your entire workflow – from data analysis to publication and rapid communication of insights to colleagues – within IPA.

Sharing and Collaborative Workspace: *Tools to facilitate research collaboration and sharing.*

IPA provides easy, flexible options for sharing biological information with colleagues. You can invite selected individuals to share particular datasets, analyses, or pathways with you, or you can utilize customized Collaboration Workspaces to share projects with specific team members within or across institutions or consortia.

Content

IPA leverages the Ingenuity® Knowledge Base, a repository of biological interactions and functional annotations created from millions of individually modeled relationships between proteins, genes, complexes, cells, tissues, drugs, and diseases. These modeled relationships, or Findings, include rich contextual details, links to the original article, and are manually reviewed for accuracy. The Ingenuity Knowledge Base provides you with a reliable resource for searching relevant and substantiated knowledge from the literature, and for interpreting experimental results in the context of larger biological systems.

Unparalleled Structure and Contextual Details
Ingenuity structures all of the biological and chemical content in the Ingenuity Knowledge Base using the Ingenuity® Ontology. By structuring the content, we enable computation and inferencing, ensure semantic and linguistic consistency, and support the integration and mapping of content from multiple sources. Unlike other ontologies, the Ingenuity Ontology is very comprehensive. This level of detail helps us capture relevant contextual details from the literature such as species specificity, cell type/tissue context, site and type of mutations, direction of change, post-translational modification sites, epigenetic modifications, and experimental methods used. These contextual details are what make our Findings different from other solutions that only report on simple "A to B" relationships. Ingenuity Findings ensure that you can access knowledge and generate hypotheses that are highly relevant to your specific experimental system.

Expert Review Process for Trusted Information
All information in the Ingenuity Knowledge Base is manually reviewed by experts for accuracy and detail, and follows strict quality control processes.

Broad and Timely Content
The Ingenuity Knowledge Base is updated weekly to include information published as recently as the prior week. It is the largest knowledge base of its kind, including modeled relationships between proteins, genes, complexes, cells, tissues, drugs, pathways, and diseases. It includes information from a wide range of published biomedical literature, textbooks, reviews, internally curated knowledge (such as pathways), and a variety of trusted third party sources and databases.

Biological and Chemical Information
All of the information in the Ingenuity Knowledge Base is structured and manually reviewed. There are four types of content:

Ingenuity® Expert Findings: Experimentally demonstrated Findings that are manually curated for accuracy and contextual details from the full-text of articles in top journals.

Ingenuity® ExpertAssist Findings: Manually reviewed, automatically extracted Findings from the abstracts of a broad range of recently published biomedical journals.

Ingenuity® Expert Knowledge: Ingenuity-modeled know-ledge such as signaling and metabolic pathways, drug/target/disease relationships, toxicity lists, and more.

Ingenuity® Supported Third Party Information: Manually reviewed content from selected sources and databases.
The Findings in IPA include modeled relationships between chemicals, proteins, genes, complexes, cells, cellular compo-nents, 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 including for drugs and candidates in all phases, from early human studies (Phase 0) to postmarket studies for alternative indications/long term safety assessment (Phase IV)

- Knowledge of genes, proteins, and compounds associated with thousands of diseases, including gene to disease associations involving SNPs and clinical biomarkers associated with over 230 diseases

- 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

- Experimentally demonstrated and predicted microRNA-miRNA binding relationships with related biological context to 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, neurological diseases, metabolic disorders, and immune disorders

- Millions of Findings extracted from the scientific literature that describe molecular interactions and regulatory events

Discover the power of IPA®

Register for a free, two week trial at:

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, and the United Kingdom. Ingenuity was founded in 1998 and is headquartered in Redwood City, California, with distributors in Australia, Japan, Korea, Singapore, and Taiwan.