

## Sole Source Justification for IPA®

QIAGEN N.V. is the sole developer, provider and source of Ingenuity Pathway Analysis (IPA®) software.

### IPA Overview

IPA® is an all-in-one, web-based software application that enables researchers to analyze, integrate, and understand data derived from gene expression, microRNA, and SNP microarrays; phosphoproteomics, 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. IPA has been cited in over 25,000 peer-reviewed journals.

### Market Leading Pathway Analysis

Unlock the insights buried in experimental data by quickly identifying relationships, mechanisms, functions, and pathways of relevance.

### Predictive Causal Analytics

Powerful causal analytics at your fingertips help you to build a more complete regulatory picture and a better understanding of the biology underlying a given gene expression study.

### NGS/RNA-Seq Data Analysis

Get a better understanding of the isoform-specific biology from RNA-Seq experiments.

### How IPA Can Be Used

IPA can be used for a variety of research goals, in multiple therapy areas, and with different data types.

Diverse Therapy Areas: Oncology, Cardiovascular Disease, Neuroscience, Metabolic Disease, Inflammation/Immunology, and Infectious Disease among others.

Broad Research Goals: Basic, Translational, Drug Discovery and Development Research

Multiple 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/GeneExpression, 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, 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, UCSC Human Isoform IDs (hg 18 & hg 19), UniGene, UniProt/SwissProt Accession.

Numerous Species-specific identifiers supported in IPA:

- Human
- Mouse
- Rat
- Additional species supported via Ortholog mapping

Model, analyze, and understand the complex biological and chemical systems at the core of life science research with IPA.

Discovery: Understand molecular mechanisms of disease to accelerate target identification and validation.

Toxicology: Elucidate biological mechanisms of drug action and toxicity.

Biomarkers: Identify and prioritize novel biomarkers by understanding role in disease pathways and involvement in clinical trials.

Pharmacogenomics: Understand mechanisms behind differential response to drugs.

Biological search: Search the scientific literature in a targeted way to find insights most relevant to an experimental question.

Pathway modeling: Build dynamic, interactive pathways to better understand research systems.

Data analysis: Quickly analyze gene expression, SNP microarray, phosphoproteomics, and other 'omics datasets to identify key insights.

Collaboration: Leverage dynamic reports, emails, and workspaces to share and collaborate with colleagues.

Integration: Directly link third-party or in-house applications, documents, and reports to the biological and chemical content and analysis capabilities in IPA

## INGENUITY KNOWLEDGE BASE

### How is IPA Different from Other Products?

The Knowledge Base is distinctive because of the breadth of biological and chemical knowledge, accuracy and structure of the content for relationship and computation using the Ingenuity Ontology.

### Not Just Simple “A to B” Relationships

Contextual details 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 are included. These contextual details allow you to ask questions such as “transcription factor X increases expression of a gene Y in a specific cell type.”

### Supports Computation

The Ingenuity Ontology makes information computationally accessible so you can more rapidly infer novel insights from your own data or get to specific knowledge that is relevant to your research. Ask questions across various types of connections (molecular, cellular, and organismal) and make inferences from one concept to another or find likely paths between molecular concepts (gene to disease, drug to gene, etc.).

### Provides Synonym Resolution

The Ingenuity Ontology ensures semantic and linguistic consistency across concepts. The Ingenuity Knowledge Base incorporates processes to resolve synonyms and homographs in order to maintain object identity and remove duplicate objects. Because the same terms are mapped across databases and concepts, you can integrate disparate information from unrelated disciplines and sources in order to run powerful queries and get precise answers to complex, data-driven questions. It also allows you to take information from multiple sources and related it to your own dataset or questions of interest.

### Content Acquisition

Content Acquisition consists of a robust set of people, processes, and technology for curating high-quality scientific relationships from peer-reviewed journals and both public and private biomedical databases. Information collected goes through a thorough, repeatable quality control process to insure the molecular information, called Findings, are captured as originally published and are integrated into the Ingenuity Ontology, a framework for organizing and describing biological evidence. Both confirmation and contradictory Findings are captured, including the source publication and the context for the Finding, to ensure users will have all the supporting evidence required to assess the applicability of a specific Finding.

### Expert Review Process

Our unique knowledge acquisition processes and quality control steps enable the level of structure in the Ingenuity Knowledge Base. All information in the Ingenuity Knowledge Base is manually reviewed by experts to ensure that the content is accurate and detailed, so whether you are using a manually curated relationship from the literature or a relationship described in a third party database, you can trust the quality of information in the Ingenuity Knowledge Base. And you can always link back to the original finding in the original source article.

**Reference:** Causal analysis approaches in Ingenuity Pathway Analysis.

Krämer A, Green J, Pollard J Jr, Tugendreich S.

Bioinformatics. 2014 Feb 15;30(4):523-30. doi: 10.1093/bioinformatics/btt703. Epub 2013 Dec 13.

## **OTHER DIFFERENTIATORS**

IPA offers several other unique advantages that make it widely considered the best software in its class.

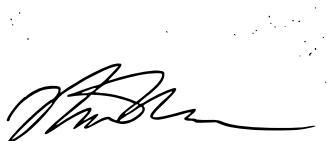
**IPA IS THE INDUSTRY STANDARD.** Since its launch in 2003, IPA has been adopted by all major pharmaceutical companies and hundreds of leading biotech, academic, and government institutions.

**IPA IS EASY TO USE.** IPA has been designed to meet the needs of biologists and chemists in addition to computationally-oriented researchers. While other tools remain limited to use by bioinformaticians, IPA has been adopted by thousands of scientists across various therapeutic areas. QIAGEN strongly believes that pathway-based analysis is the domain of all researchers and IPA has been developed so that it is intuitive to use, easily integrated with other tools (including proprietary ones) and includes relevant and accessible features.

**IPA IS A COMPREHENSIVE SOLUTION.** Ingenuity believes that it is critical for a pathway solution to reflect functionality across a range of key domains, including transcriptomic, proteomic, and metabolomic data analysis for key drug discovery initiatives such as molecular toxicology and biomarker discovery. Unlike other pathway tool vendors who separate this capability among different product offerings, all this functionality is integrated within IPA.

**IPA ENABLES A DYNAMIC VIEW OF BIOLOGICAL AND CHEMICAL SYSTEMS.** In addition to its unique pathways analysis algorithms and marketing leading library of well characterized pathways, IPA also offers a powerful suite of tools which enable users to dynamically grow, expand, or narrow their view of a pathway and create customized and relevant representations of the system.

**IPA IS SUPPORTED BY A WORLD CLASS COMPANY.** Headquartered in the heart of Silicon Valley, Ingenuity has since 1998 (and continuing after acquisition by QIAGEN in 2013) built a global team of responsive scientists, software developers, and PhD level technical and customer support scientists who work together to enable the research of our customers around the world. QIAGEN consistently incorporates the feedback of our customers into our product development cycles and provides comprehensive product support and a wide variety of training options to all users.

A handwritten signature in black ink, appearing to read "Stuart Tugendreich".

Stuart Tugendreich, PhD  
Director and Global Product manager, IPA Product Line