

## **197g Knowledge-Based Computational Pathways Analysis for Integrative Drug Discovery**

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The Ingenuity Pathways Knowledge Base (IPKB) is the world's largest curated database of biological networks created from millions of individually modeled relationships between proteins, genes, complexes, cells, tissues, drugs, and diseases. At the core of this resource are a highly-structured life sciences ontology and an enterprise knowledge management system that enable large-scale high-fidelity acquisition and structuring of scientific content that is scientifically accurate, semantically consistent, contextually rich, broad in coverage, and up-to-date. Using the IPKB, bioinformaticians can develop genome-scale computational solutions for understanding biological mechanisms. We have used this platform to further develop Ingenuity Pathways Analysis, a systems biology application for computational analysis of high-throughput experimental datasets. Network models of biomolecular pathways are computationally generated from the IPKB and sets of significantly expressed genes from proteomics and microarray datasets, and are further annotated with functional and physical relationships such as gene regulations, protein-protein interactions, post-translational modifications, and drug-target interactions. Our approach has been successfully applied to biological data analysis throughout the drug discovery process, from early stage target ID and validation, to later stage activities such as toxicology, pharmacogenomics, biomarker identification, and alternative indications of approved drugs. We describe how ontologies and semantically-structured knowledge can provide a powerful foundation for novel collaboration and discovery at the interface between chemistry and biology.