



THE ICONIX EXTENSIBLE INFORMATICS SYSTEM (IXIS™)

VERSION 6.0 FEATURES AND REQUIREMENTS

The Iconix Extensible Informatics System (IXIS™) is a multi-dimensional data capture, analysis, visualization and reporting software system initially developed to support DrugMatrix[®], the world's largest toxicogenomics database of microarray and pharmacology data. The software can be licensed and customized for use with any proprietary multi-dimensional datasets. The base system is scalable and flexible, built on a technology base that includes an Oracle database schema, a BEA Weblogic[®] Java™ application server and a Tibco General Interface™ user interface. IXIS supports the needs of toxicologists, pharmacologists, chemists and drug discovery scientists. Additional data types, such as proteomics and metabonomics, can easily be added to support all aspects of pharmaceutical R&D.

BENEFITS

Easily integrate data from multiple sources

Compound characteristics	Structures, physical properties, structural relationships, links to associated target genes and annotations from the clinical literature.
Gene expression data	Control and treatment groups, multiple tissues, doses and timing.
<i>In vivo</i> and <i>in vitro</i> data	Body and organ weights, animal observations, histopathology, clinical chemistry and hematology.
Genomic information	Gene names, synonyms, symbols, functional annotations and links to public databases.
Molecular pharmacology data	Receptor binding, channel binding and enzyme inhibition assays, connections to constituent genes.
Metabolic, signaling and toxicological pathways	With links to component genes.
Drug Signatures [®]	Gene expression-based biomarker sets predictive of <i>in vitro</i> or <i>in vivo</i> responses.

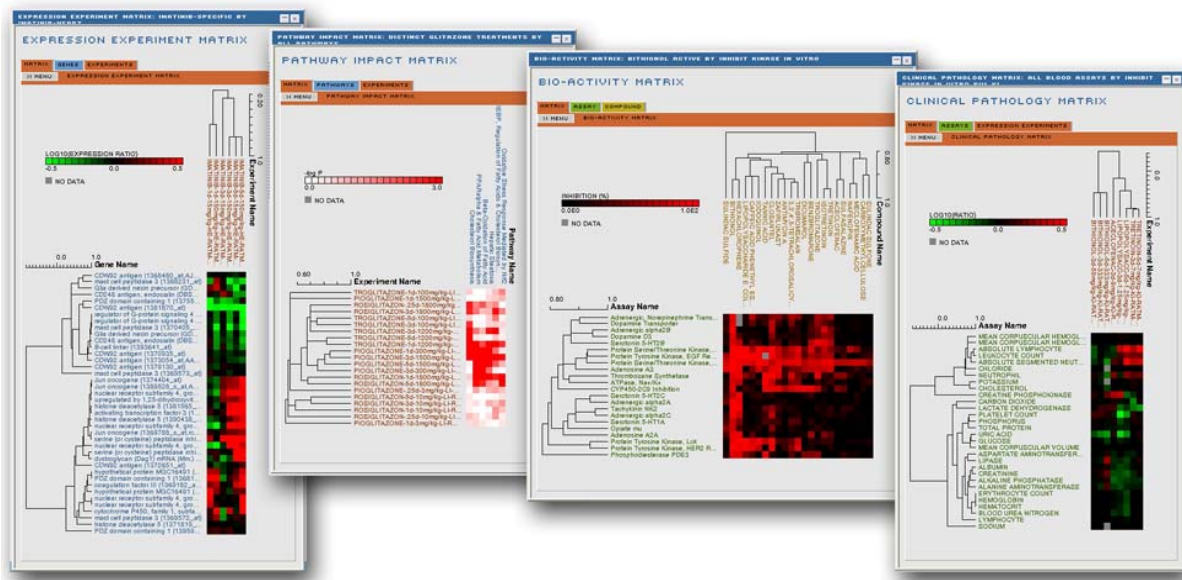
Perform novel analyses only possible in an integrated system

Compare expression profiles	Which have similarities?
Analyze Drug Signatures	Do any predict liabilities?
Compare gene lists	Do different drugs induce similar changes in gene expression?
Analyze gene ontology terms	Do the perturbed genes point to a mechanism of action?
Identify common and divergent changes within a set of gene expression experiments	What is the common mechanism of action?
Assess pathway impact	Which pathways are changed?
Overlay expression changes on pathway maps	Is there an impact on the biology?
Analyze pathway response chart	How extreme are the pathway changes?
Assess extent of hierarchical clustering	Which patterns of gene expression, molecular pharmacology, clinical chemistry, hematology or Drug Signature scores relate drug treatments?

Leverage existing resources

Oracle schema	<ul style="list-style-type: none">• Enhances interoperability with your existing databases• Copy data from your histopathology or gene expression databases to IXIS
ISIS compatible	Supports molecular structure database searches
Standards support	Interfaces with other data analysis tools (e.g., Spotfire)

EXAMPLE FEATURES

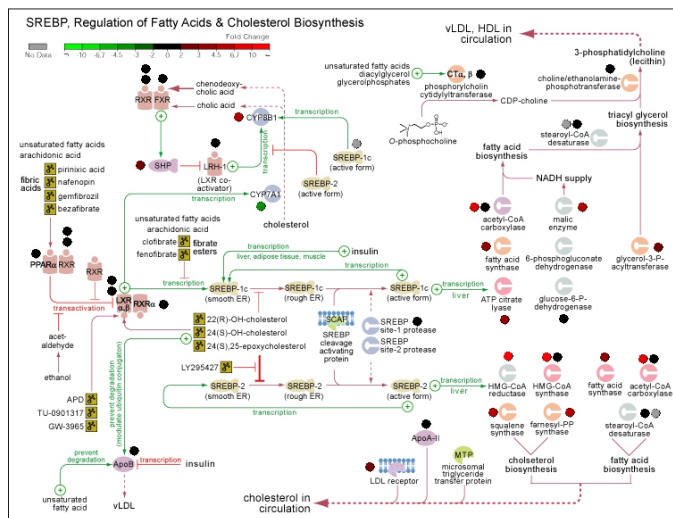


Hierarchical Clustering (top)

The many integrated information domains in IXIS enable the analysis of diverse types of data using common analytical methods. Gene expression data are hierarchically clustered and displayed in a gene expression matrix heat map. Similar analyses can be performed on clinical chemistry, hematology, molecular pharmacology and Drug Signature biomarker sets. This diverse set of tools allows one to identify patterns and relationships not easily discerned in other systems.

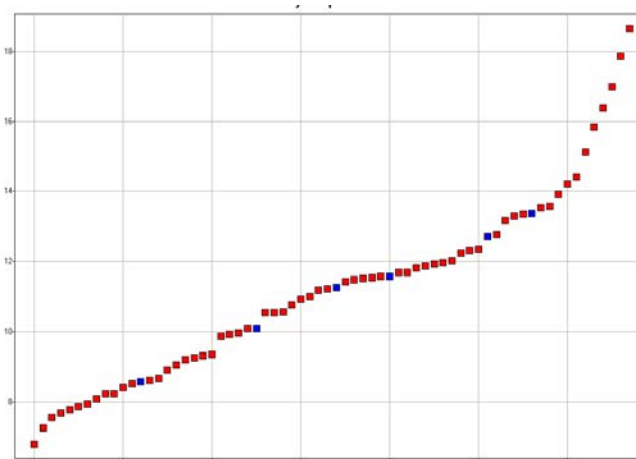
Pathway Impact (middle)

By integrating biological pathway information with gene expression data, IXIS supports global visualization of the impact of compound treatment effects on gene expression in affected pathways. Researchers can quickly identify pathways relevant to both efficacy and safety.



Pathway Response Chart (bottom)

The IXIS system is optimized to identify trends within the global dataset. By integrating with standard visualization tools such as Spotfire, IXIS can display a ranking of all experiments relative each other, based on the transcriptional response of component genes. Experiments of interest (blue squares) can be identified within the trend.



FULLY CUSTOMIZABLE

Feature	Description	Administration
Simple Search	Search for any item by name, and synonyms, symbols and identifiers are automatically included. Example: find drug “Lipitor” retrieves “Atorvastatin”	Search can be configured to include multiple namespaces in the database simply by adding metadata.
Advanced Query	Search for any item based on one or more annotations or properties. Supports filtering and multiple “and” logic. In combination with the list manipulation tools, any complex logic can be executed. Example: find drugs that inhibit HMG CoA Reductase with an IC ₅₀ less than 10 nM AND that induce transcription of genes in the Cholesterol Biosynthesis pathway greater than 2-fold.	Flexible dynamic query builder can be extended to new data types by editing XML in the graphical user interface (GUI) codebase. A toolbox with hundreds of specific queries is available, from which an infinite number of combinations can be built.
Workspaces and Lists	Search results are saved in private user workspaces. Results can be displayed, edited and imported into analytical tools.	The user workspaces and lists are stored on the server, allowing transparent use from any computer. Workspaces are administered by each user through a GUI.
List Combinations	Lists can be combined using Union, Intersect and Subtract tools. These, in combination with the Advanced Query tool, allow an infinite number of logical queries to be built in the GUI. Example: find genes that are induced by Clofibrate that are not induced by Fenofibrate.	List management is built into the base system.
Import/Export	Lists of interesting results can be emailed to colleagues, who can import the list into their own workspaces for review. Example: a publication reports a 10-gene biomarker for hepatotoxicity. A text file with the probe set names for all 10 genes can be imported into an IXIS list and sent for review. Queries can be run to search the database for similar patterns.	Import/Export is built into the base system.
Browsing Data	With one click, a web-based interface presents all information related to an item identified in search results. Example: Viewing the gene for HMG CoA Reductase, a scientist can access all of the associated names and symbols, Gene Ontology terms, experimental conditions that induce and repress that gene, other genes that are co-regulated, pathways containing the gene and drugs designed to interact with the gene product.	The base system supports 8 data dimensions: gene, compound, assay (clinical and pharmacological), expression experiment, expression study, signature, histopathology and pathway. The data model and user interface can be easily extended to add new dimensions, e.g., proteomics.
Scalability	The IXIS platform has been used with databases of over 50 million records with good interactive performance.	A dataset of 50M records requires about 100GB of Oracle disk space and 2GB of application server RAM. Increasing the dataset size increases the system requirements in a linear relationship.

SYSTEM REQUIREMENTS

Component	Hardware Requirements	Software Requirements
Client Workstation	<p>Computer: PC</p> <p>Minimum processor: 700 MHz Pentium III (1GHz or faster) or AMD equivalent</p> <p>Operating System: Microsoft Windows 2000 or XP</p> <p>Minimum monitor resolution: 1024 x 768</p> <p>Minimum RAM: 256 Mb</p>	<p>Microsoft Internet Explorer 6.0 or newer</p> <p>To enable MDL copy/paste for structure queries, Chime Pro 2.6 SP4 or newer must be licensed from MDL Information Systems.</p> <p>To enable IXIS copy/paste into other chemical structure software, Chime 2.6 SP4 or newer must be installed (free from MDL Information Systems at: www.mdli.com/downloads)</p>
Single Server Configuration	<p>The XIS installation can be supported on a single server or two servers (separate Web and Oracle servers). Separate servers are recommended for higher performance in multi-user environments. The single server configuration must meet the greater of the requirements for the individual Web and Oracle servers.</p>	
Web Server	<p>Computer: Sun, with DVD reader</p> <p>Minimum processors: 2 x 450 MHz Ultraspac III</p> <p>Operating System: Solaris 2.8 or newer</p> <p>Minimum storage: 20 Gb disk (dual mirrored drives recommended)</p> <p>[Note: a high-performance Intel or AMD server running Linux may be used; please inquire for specific requirements]</p>	<p>BEA WebLogic Server 10 (must be licensed from BEA Systems)</p> <p>Java JDK 1.5 or newer</p>
Oracle Server	<p>Computer: Sun, DVD reader</p> <p>Minimum processors: 2 x 750 MHz Ultraspac III (dedicated to IXIS; if other applications are also run on the server, a more powerful server is recommended)</p> <p>Operating System: Solaris 2.8 or newer</p> <p>Minimum storage: High performance Ultra SCSI II RAID disk system with 120Gb free space (RAID Level 5, Fiberchannel I/O recommended)</p> <p>Minimum RAM: 4 Gb</p> <p>[Note: a high-performance Intel or AMD server running Linux may be used; please inquire for specific requirements]</p>	<p>Oracle 10g (must be licensed from Oracle)</p> <p>To enable structure searches, ISIS RCD must be licensed from MDL Information Systems.</p>
Oracle Level Security	<p>Implemented through the standard mechanisms supported by Oracle 10g.</p>	
Application Server Security	<p>Can be configured to use any of the following authentication methods:</p> <ul style="list-style-type: none"> • Passwords stored in an Oracle table as free text • Passwords store in an Oracle table as encrypted passwords • Integration with an existing LDAP authentication server 	