



## ToxShield™ Suite

### Gene Logic introduces ToxShield™ Suite, a new paradigm in predictive toxicogenomic software systems.

Gene Logic's expertise in microarray data generation, predictive toxicogenomic analyses, and interpretation of customers' compounds has facilitated the discovery and validation of accurate markers of toxicity. Now you can quickly access our toxicogenomics information to screen and rank your compounds, providing toxicologists and lead optimization scientists in your organization with specific information to enhance their decision making process.



#### ToxShield™ Suite enables you to:

- Expand your internal knowledge base of toxicogenomic marker response across diverse compounds.
- Rank candidate leads within and between compound series using toxicity assessments provided by validated predictive models.
- Assess the likelihood that the reported pathology will occur by observing the probability scores.
- Compare the compound's predictive profile to a large database of reference compound profiles.
- Identify new or additional clinical pathology parameters that may need to be included in downstream preclinical studies.
- Confirm drug candidate choices.
- Develop screening assays for related compounds or chemical series based on Gene Logic's toxicity markers.

#### ToxShield™ Suite also addresses difficult questions such as:

- Is the compound likely to be a human toxicant?
- What type of injury will it likely induce in humans or rats?
- What reference compounds does it most closely resemble at the level of gene expression?
- Is there a time and dose relationship with this compound at the level of gene expression?

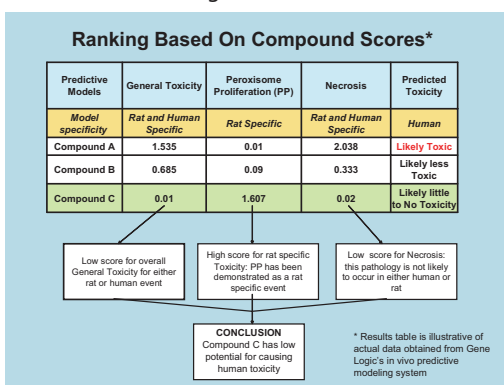
With ToxShield™ Suite, you can analyze your data directly using secure, web-based software or fully deployed on-site system behind your firewall to predict potential toxicity in humans based on rat Affymetrix GeneChip® data. This easy, intuitive workflow yields a comprehensive report in as little as 2-4 hours (e.g. when starting with up to 20 CEL files from either Affymetrix Rat Genome 230 2.0 or Rat Genome U34A Arrays)!

#### The resulting ToxShield™ Prediction Report contains:

- Multiple levels of information that further characterize and assess your compounds' toxicity potential
  - Overall Toxicity Determination: Toxic/Non-toxic
  - Toxicity relevant pathology categories: Multiple categories based on specific organ toxicities have been defined and tested
  - Compound similarities: ToxShield™ Suite matches your compound profile to those within the ToxExpress® System and reports the top matches
- Visualizations that relate findings from your compound to well-characterized reference compounds and provide a critical link to well understood biology
  - Distribution profiles relate your compounds' gene expression profile to reference toxicants, negative control compounds, and vehicles
  - Probability measurements of your sample or sample cohorts for a toxic response or pathology specific response align with distribution profiles
  - Bar charts provide a continuum of response from negative to positive and represent how each of the reference compounds is measured by the individual models
  - Heat maps relate your compounds' profile to selected compound classes providing a closeness of fit measure

## Example of rank ordering candidate leads

A rank ordering feature is an integral part of the software. To invoke a multiple compound comparison, simply select the compounds and click on the Cross-Project function. Compounds will be compared to each other relative to their toxicity scores for each predictive model. The analysis then rank orders based on these scores as illustrated in the diagrams below:



Marker responses can change between and within compound classes and series. ToxShield™ Suite enables user to begin understanding how Gene Logic's proprietary markers respond to different compounds. With as little as three compounds, users can begin building internal knowledge of these responses and determine those that may be best for bioassay screening applications. These bioassays can be gene expression based or other acceptable formats including ELISA and qRT-PCR and can be customized for specific research activities in drug discovery.

## Markers Contribution to the Toxicity Scores

| Model           | General Tox Patterns | PP Patterns          | Necrosis Patterns    |
|-----------------|----------------------|----------------------|----------------------|
| Compound A      | Samples 1-3<br>↑ ↑ ↑ | Samples 1-3<br>↓ ↓ ↓ | Samples 1-3<br>↑ ↑ ↑ |
| Overall Pattern | ↑ ↑ ↑                | ↓ ↓ ↓                | ↑ ↑ ↑                |
| Marker 1        | ↑ ↑ ↑                | ↓ ↓ ↓ (D)            | ↑ ↑ ↑                |
| Marker 2        | ↑ ↑ ↑ (D)            | ↓ ↓ ↓                | ↑ ↑ ↑ (D)            |
| Marker n...     | ↑ ↑ ↑                | ↓ ↓ ↓                | ↑ ↑ ↑                |
| Compound B      | Samples 1-3<br>↓ ↓ ↓ | Samples 1-3<br>↑ ↑ ↑ | Samples 1-3<br>↑ ↑ ↑ |
| Overall Pattern | ↓ ↓ ↓                | ↑ ↑ ↑                | ↑ ↑ ↑                |
| Marker 1        | ↓ ↓ ↓ (D)            | ↑ ↑ ↑                | ↑ ↑ ↑                |
| Marker 2        | ↓ ↓ ↓                | ↑ ↑ ↑ (D)            | ↑ ↑ ↑ (D)            |
| Marker n...     | ↓ ↓ ↓                | ↑ ↑ ↑                | ↑ ↑ ↑ (D)            |
| Compound C      | Samples 1-3<br>↑ ↑ ↑ | Samples 1-3<br>↓ ↓ ↓ | Samples 1-3<br>↓ ↓ ↓ |
| Overall Pattern | ↑ ↑ ↑                | ↓ ↓ ↓                | ↓ ↓ ↓                |
| Marker 1        | ↑ ↑ ↑                | ↓ ↓ ↓ (D)            | ↓ ↓ ↓ (D)            |
| Marker 2        | ↑ ↑ ↑ (D)            | ↓ ↓ ↓                | ↓ ↓ ↓                |
| Marker n...     | ↑ ↑ ↑                | ↓ ↓ ↓                | ↓ ↓ ↓                |

The most contributing markers to the Toxicity Score based on magnitude and direction of change are illustrated. Marker response can be monitored over multiple compounds to help determine which are ones useful in screening applications.

(D) Indicates this pattern is different from the Overall Pattern. This marker may offer little in terms of screening.

## ToxShield™ Suite Availability

ToxShield™ Suite is available as an enterprise-wide web application or as a fully deployed server application. The user interface will support multiple prediction model systems; however, the initial release of this software contains *in vivo* rat liver predictive models.

## Predictive Toxicogenomic Model Validation

The Predictive Models used to generate the results have been extensively validated using a widely-accepted statistical cross-validation method including complete removal of whole compound studies (compound-drop validation). This approach is very stringent and provides an accurate estimate of the success rate seen using naive data. In each of these analyses, the models are rebuilt after the study samples have been removed and markers are re-selected before the removed data are used as naive test data.

## ToxShield™ Suite Requirements

ToxShield™ Suite requires Affymetrix GeneChip® Data and is optimized for small molecules.

The web-based application requires the following software:

- Microsoft Internet Explorer version 6.0 or later or Netscape Browser version 7.0 or later.
- The Java Runtime Engine version 1.4.2\_05 or later
- The Adobe SVG Viewer version 3.01

All communication and data transfer with Gene Logic web servers take place via 128-bit secure socket layer (SSL).

## For More Information

Visit Gene Logic's website at [www.genelogic.com](http://www.genelogic.com). Please e-mail [info@genelogic.com](mailto:info@genelogic.com) or call 1-800-GENELOGIC to have a Gene Logic representative contact you, or contact your Business Development representative.



[www.genelogic.com](http://www.genelogic.com)

610 Professional Drive • Gaithersburg, Maryland 20879 • Tel: 1.800.GENELOGIC • Fax: 301.987.1701 • Email: [info@genelogic.com](mailto:info@genelogic.com)

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