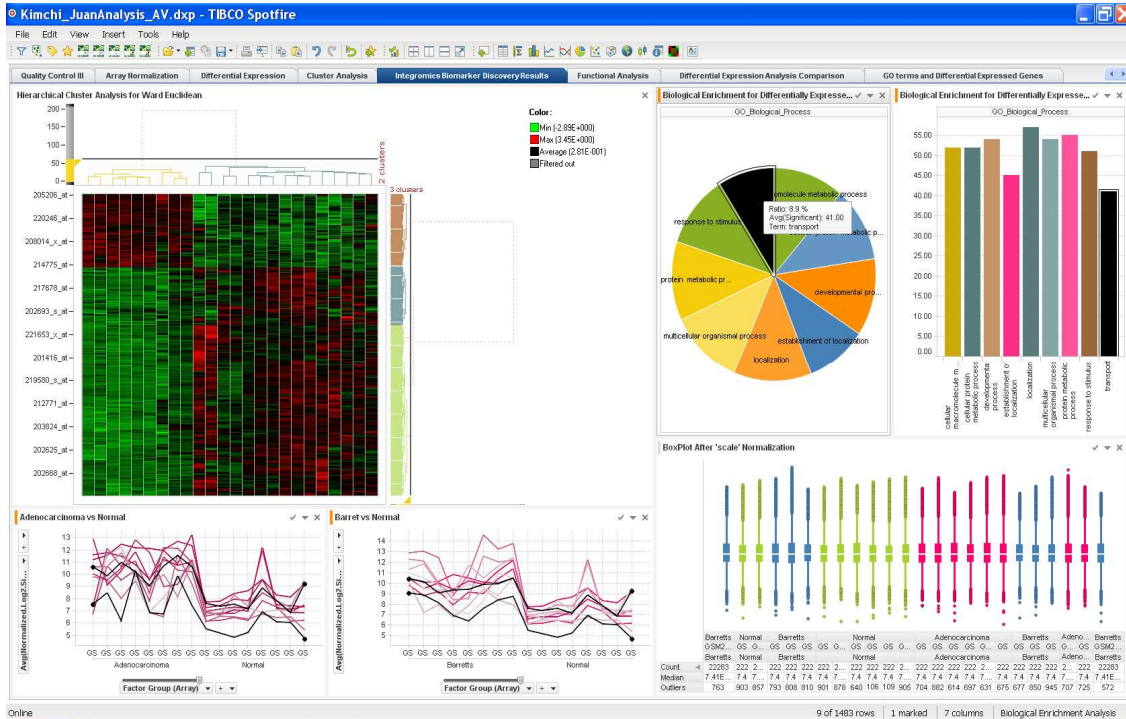


INTEGROMICS BIOMARKER DISCOVERY™ for TIBCO Spotfire

Advanced Microarray Data Analysis Software

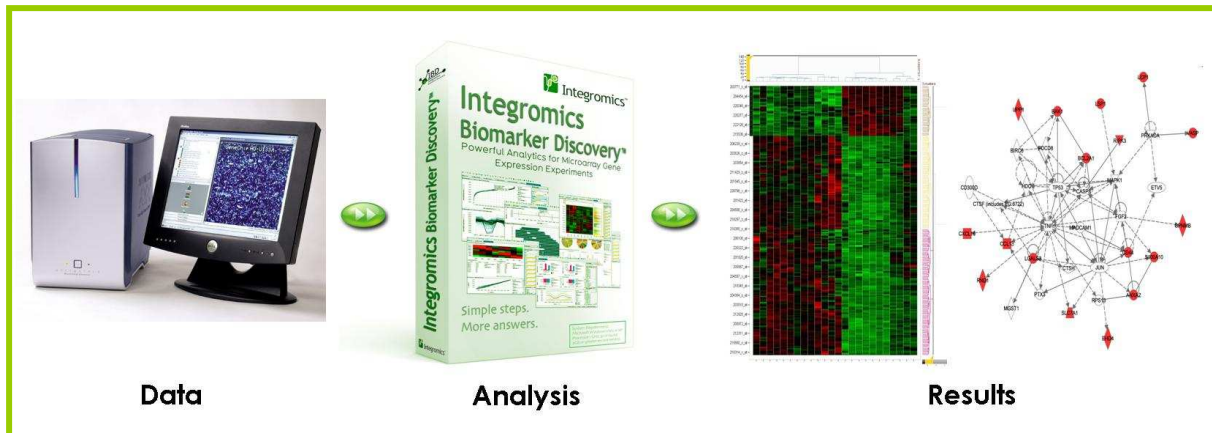


- **Ease-of-use.** Identify outliers, patterns and unanticipated relationships in your genomic data.
- **Reproducibility.** Intuitive workflow to perform statistical analysis for differential expression of genes.
- **Flexibility.** Dynamic and linked visualizations ensure optimal end-user experience.
- **Biological Significance.** Extract biological knowledge from annotation on gene ontologies and pathways.
- **Fast Results.** Summarize your results and create publication-ready reports in minutes.

Introduction

During the last decade, biomedical researchers have experienced a tremendous revolution in the way in which they analyze living organisms at a molecular level. This revolution, which can be compared to the appearance of the cloning techniques during the 70's, has been possible due to the development of new high-throughput experimental techniques.

The so called “-omics” technologies comprise a set of tools and methods that allow researchers to better understand the diverse properties of genes thus giving a global picture of biological systems in a wide range of studies, such as tumor classification, biomarker and drug discovery.



As a result, the need for high quality and high-throughput gene expression data analysis is growing, especially in biomarker validation and clinical research. All such studies require sophisticated data analysis methods, capable of managing the complexity of multi-gene, multi-sample projects, and returning reliable biological information.

Integromics Biomarker Discovery™ (IBD) for TIBCO Spotfire is a custom bioinformatics application that is focused on preprocessing, normalization and interpretation of raw microarray gene expression data. As part of TIBCO Spotfire, IBD offers a new visual and intuitive way to interact with the data, answer any question on demand, interactively filter data, automatically calculate and recalculate cross-tables and graphs, and produce reports of results.

It provides users with analysis workflows for biomarker discovery in the fields of gene expression and CGH data analysis. There are specific workflows for the main gene expression platforms: Affymetrix and Two-Channel as well as a flexible integration of all included

analytical methodologies that will allow the analysis of other type of data beyond gene expression. Additionally, state of the art data mining tools are available for the integrated analysis of experimental and functional data (e.g. gene annotations). Throughout the analysis process, the step-by-step guide facilitates statistical analysis making it possible for user of all levels to produce meaningful and reliable results.

Step-by Step Workflow

Integromics Biomarker Discovery™ (IBD) for TIBCO Spotfire® has an easy-to-use workflow that integrates advanced statistics and

interactive visualizations to extract biological signals and draw reliable conclusions from differentially expressed genes. Designed for high-throughput genomic studies- the workflow guides the data analysis from start to finish.

Steps of the analysis include:

Importing Microarray Data

This step includes selecting a platform, importing the data, creating an experimental design, performing probe level analysis, filtering and dye swap.

Quality Control

The three steps of quality control include monitoring the quality of the raw data, determining the quality of the array replicates and examination of the signal distribution of the different arrays.

Array Normalization

Normalize data and perform fold change calculations. There are two methods used in this process: within array normalization and between array normalization.

Differential Expression Analysis

Differential expression computes the relative expression levels among hybridization groups to identify genes that are expressed differentially. There are two methods for this kind of analysis, parametric and non-parametric.

Cluster Analysis

Clustering is the classification of samples into groups. This step enables the user to perform hierarchical clustering.

Functional Analysis

Functional analysis is used to gain information about the biological processes affected by the experiment. IBD offers two options for functional analysis: Annotation and Biological Enrichment.

Ingenuity Pathways Analysis (IPA) Integration

Ingenuity Pathways Analysis is a software application that enables biologists and bioinformaticians to identify biological mechanisms, pathways and functions most relevant to their experimental datasets and genes of interest.

Benefits of Integromics Biomarker Discovery™

1. Support for common commercial array platforms
2. Enhanced human-data interaction with an easy-to-use guided workflow
3. Powerful statistics and interactive visualizations
4. Functional annotations and biological enrichment analysis
5. Ingenuity Pathway Analysis (IPA) Integration
6. Worldwide technical support

Support for common commercial array platforms

Integromics Biomarker Discovery™ accepts Affymetrix CEL files, or tab-delimited text files, including the standard output from Agilent CGH, Agilent Two-Channel Gene Expression, Genepix, QuantArray, ScanArray, SMD and Spot arrays.

Enhanced Human-Data Interaction with an Easy-to-Use Guided Workflow

It is critical to ensure the reproducibility of the results and conclusions by carefully tracking the analysis steps. Too often it is impossible for an independent group to repeat the same analysis using the same data - reducing the consistency and impact of the results. During the analysis, a strict workflow should be followed to minimize inconsistencies or errors from discretionary criteria or input of humans in the process.

Integromics Biomarker Discovery™ enables the users to follow a structured yet flexible process which will allow obtaining reliable and reproducible results. All steps in the Guide include a Help icon that explains all software features, and users are guided through the easy workflow. The workflow enables the user to analyze the data tables, while linked to the

TIBCO Spotfire powerful graphical and reporting capabilities for statistical analysis.

The user can go back and forth within the workflow, conducting various strategies and recalculating the results. It is also possible to perform a user driven analysis using the Tools to redesign and customize the workflow.

Powerful Statistics and Interactive Visualizations

Differential expression aims at computing the relative expression levels among hybridization groups. Methods are both for parametric and non-parametric data.

Explore Functional Annotations and Biological Enrichment

The functional analysis provides information concerning the Biological Processes, Cellular Components and Molecular Functions associated with the list of those genes appearing as differentially expressed under the conditions studied. Different significance parameters are provided with the results obtained, allowing the user to filter and keep only those significant biological functionalities associated to the set of genes of interest.

Ingenuity Pathways Analysis (IPA) Integration

Ingenuity Pathways Analysis (IPA) is a web-based software application that enables users to identify the biological mechanisms, pathways and functions most relevant to their experimental datasets or genes of interest.

Integromics Biomarker Discovery™ directly integrates with IPA allowing users to:

1. Understand microarray results in a biological context. Rapidly identify pathways, molecules, or diseases related to the respective data.
2. Analyze changes in biological states across time and dosages
3. Create customized pathways for their targets, biomarkers, processes, and diseases of interest
4. Integrate proprietary biological relationships into IPA pathways
5. Analyze customized pathways to derive biological function
6. Compute "shortest paths" between genes or sets of genes
7. Search literature to access information on genes, pathways, or diseases
8. Easily create customized, publication quality graphics

The Ingenuity Pathways Knowledge Base is the world's largest database of biological networks created from millions of individually modeled relationships between proteins, genes, complexes, cells, tissues, drugs, and diseases. For more information visit:

<http://www.ingenuity.com/>

Worldwide Technical Support

Unlike existing freeware, Integromics provides worldwide support for IBD customers. For more information, contact: support@integromics.com

Product Literature

For more information on Integromics Biomarker Discovery™ Software, visit: www.integromics.com/IBD.php

For an example of how Integromics Biomarker Discovery™ is used in the laboratory, please view the recorded webinar, “Microarray Data Analysis with Integromics Biomarker Discovery™ for TIBCO” available at:

www.integromics.com/ibd_webinar_request.php

Ordering Information

For ordering information and pricing please contact Integromics at sales@integromics.com

About Integromics

Integromics provides state-of-the-art software solutions for data management and data analysis for the Life Sciences.

From its scientific base, Integromics offers its clients a deep and current understanding of challenges, initiatives and solutions related to Life Sciences. Integromics has formed important partnerships in industry and academia to develop technological solutions that enable clients to achieve their goals.

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