Multi-Omics Analysis Software For Targeted Identification Of Key Biological Pathways

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Prevailing Paradigm for Biological Information Flow

Genomics → Transcriptomics → Proteomics → Metabolomics

Genes → mRNA → Proteins → Metabolites
Improving S/N Of Multi-omics Measurements By Integrating Prior Biological Knowledge

Aminoglycosides

• First line TB drugs, potently cidal

• Protein synthesis inhibitors that bind the 30S subunit of the ribosome and cause mistranslation and/or premature termination of protein synthesis

• Anti-mycobacterial mode of action unresolved

• Critical underlying metabolic derangements associated with cell death

• Practical importance
Merge Metabolomic and Transcriptomic Data And Analyze By Pathway

- LC/MS GC/MS
- MassHunter Qual/Quant
- GeneSpring Platform
- Pathway Architect
- Microarrays
- Feature Extraction
GeneSpring Multi-Omics Analysis For Integrated Biology

GeneSpring-GX
- mRNA
- Alternative Splicing
- microRNA

GeneSpring-GT
- Genome-wide association
- Copy Number Variation

GeneSpring-NGS
- DNA Variation
- Chromosomal Rearrangements
- RNA-Seq
- Gene Fusion Detection
- Alternative Splicing

GeneSpring-MPP
- Proteomics
- Metabolomics

GeneSpring-Pathway Architect
- Multi-omics Analysis Functionality
- Joint Pathway Analysis
- Computational Network Discovery
Pathway Architect

Canonical pathway visualization
Single or multi-omic analysis
Biochemical, metabolomic, & signaling pathways from publicly reviewed databases
- Wikipathways
- Biopax (OWL)
- GPML
- Custom - personalized

Easy pathway browsing, filtering, navigating and searching
Convenient export of compound list from pathways
BridgeDb: Mapping Entities Onto Pathways
Resolves the mapping problem between databases

Metabolites Identifiers:
- KEGG
- HMDB
- ChEBI
- CAS

Proteins Identifiers:
- Swiss-Prot
- UniProt
- UniProt/TrEMBL

Genes Identifiers:
- Entrez Gene, GenBank, Ensembl
- EC Number, RefSeq, UniGene, HUGO
- HGNC, EMBL
Multi-Omics Analysis Using GeneSpring-IB
Pathway Architect In GeneSpring / MPP

Projects

Microarray Data

LC/MS based Metabolite Abundance Measurements

Joint Pathways experiment: metabolomics / transcriptomics
Tuberculosis / Drug Metabolomic Profiling Results
Tuberculosis / Drug Transcriptomic Profiling Results
Multi-Omics Analysis In GeneSpring / MPP

- Navigable list of enriched pathways
- Pathway search by entities of interest
- Pathway filters by enrichment or count
Pathway analysis of both genes and metabolites reveals strong enrichment for specific amino acid biosynthetic pathways.
Tuberculosis / Drug Joint Pathway Analysis
Tyrosine Metabolism

Heatmap of all pathway entities, dynamically linked to pathway selection for comparative analysis

Microarray and Metabolite Data Overlay

Microarray or Metabolite Data Results

The Measure of Confidence

Agilent Technologies
Pathway Analysis Driven Experiment

Enabling hypothesis-driven experimental design by incorporating prior biological knowledge from multiple measurement technologies
GeneSpring-IB: Enabling “The Next Experiment“

Multi-Omics Analysis: Pairwise enrichment (GX, NGS, MPP)

- Gene Expression and Metabolite Abundance
- Metabolite Abundance and Protein Expression
- Gene Expression and Protein Expression
- Comparative Gene Expression (microarrays and NGS)
- Comparative Metabolite Abundance
- Comparative Protein Expression

Next Experiment:
- Pathway-directed Analysis for targeted verification of members of statistically significant pathways
Examine Data And Export Next Experiment

Export Pathway Entities

Examine Experimental Data
Pathway Architect: Target Protein List Can Be Exported To Peptide Selector In Spectrum Mill

Create list of target peptides for proteomics study
• Measure changes in protein expression level
• Detect post-translational modifications

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Paste protein accession numbers from Pathway Architect

Generate peptide lists for:
• QQQ MRM
• Q-TOF target list
Merging metabolomics and transcriptomics analyses yielded novel insights into the Tuberculosis / antibiotic response

- Detect a strong enrichment for amino acid biosynthetic pathways
- Identify unexpected aspects of aminoglycoside activity, such as methionine homeostasis
- Next step is to examine changes in proteins in targeted pathways

Protein component of interesting pathways can be examined using the export function of Pathway Architect

- Select interesting pathway(s)
- Export protein accession number list for import into Spectrum Mill
- Spectrum Mill produces a target peptide list (QQQ or QTOF)
- Import list into MassHunter Acquisition software
Thank you!