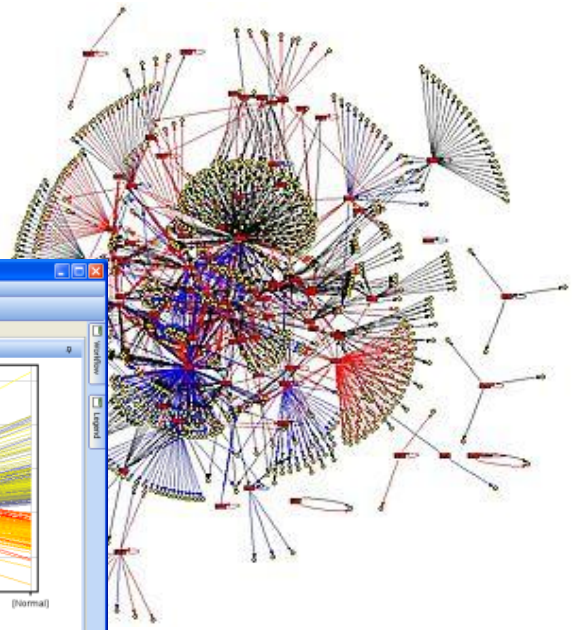
GeneSpring GX 11 and 11.5

Agilent Bioinformatics User Meeting

May 12, 2010



Michael Janis
Product Manager, GeneSpring
Agilent Technologies

We we've been…

GeneSpring GX – Solution for RNA Analysis

7800 references in Google Scholar and over 1,600 in peer reviewed publications

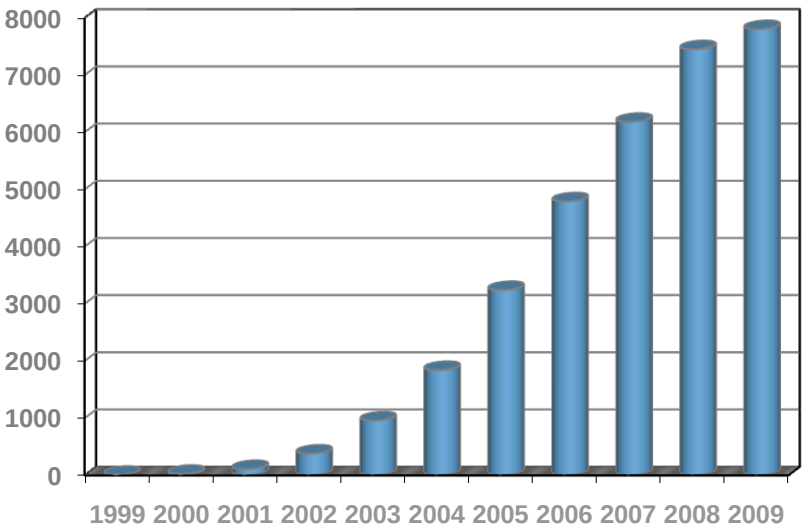
>10 years of history in RNA-based applications

Open-platform application

GeneSpring strength lies in biological contextualization

- Network building
- NLP
- GO, GSEA, and GSA analysis
- Automated biological entity translation across species or microarray platform

*April 2009



Google Scholar:
"gene expression" and "GeneSpring" = 7,800
"gene expression" and "Partek" = 551

Technical Support: 24 hrs/5 days/wk
Free 1:1 webex sessions

Where we are now
GeneSpring GX 11 Goals

To support genomic research through analysis of all biological entities- genes, variations, microRNAs, and exons - and the combination of such heterogeneous data

Goal 1: Increase usability of application

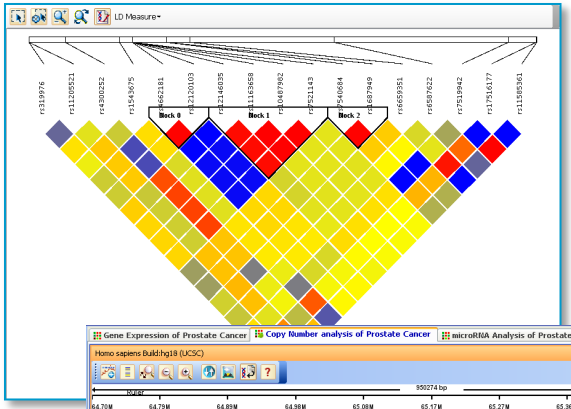
Goal 2: Expand support to DNA-based applications

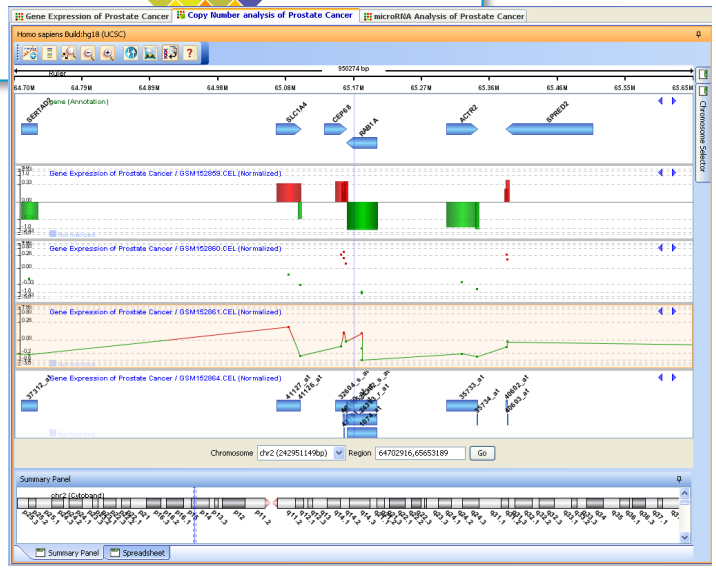
- Genome-wide association studies
- Copy number variation analysis

GeneSpring – Release Features v11

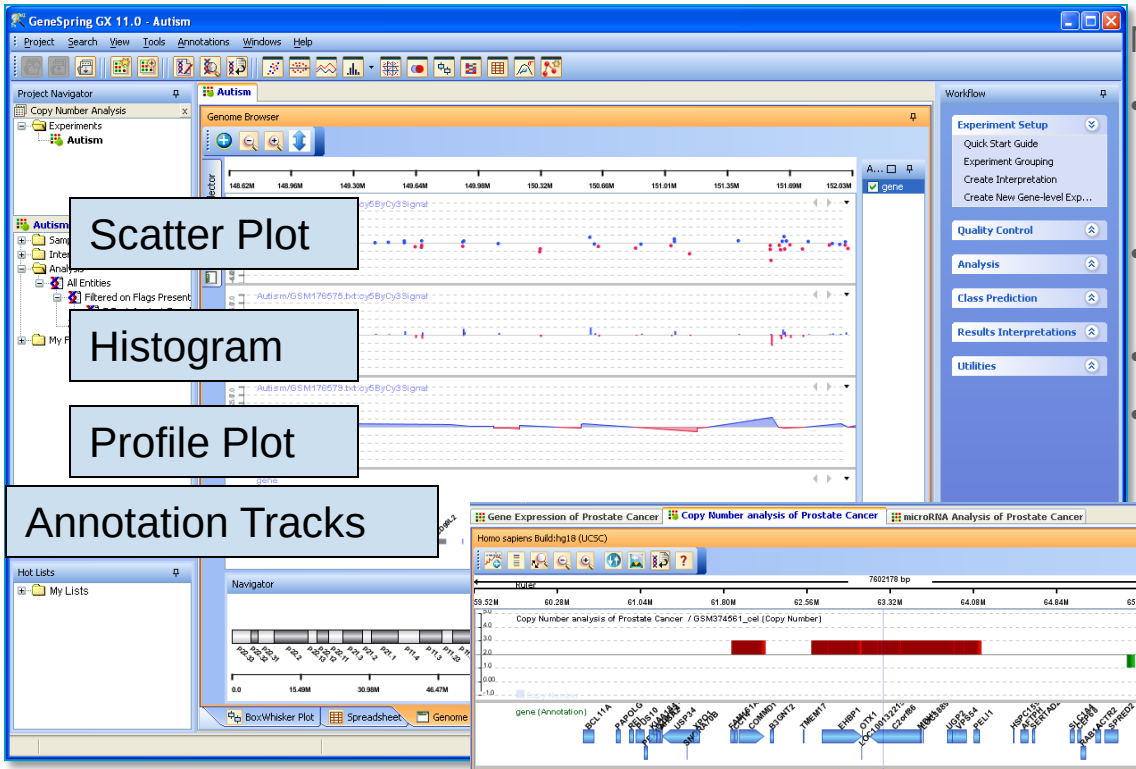
GS 11 (2009) – New features		
Mac OS X 64-bit support	**Genomic Copy Number analysis**	**Association analysis with genotyping data**
Create Gene-level experiment from probe-level data	Circular Binary Segmentation for CN	BRLMM/Birdseed for genotyping
NCBI GEO Importer	HMM for LOH	EIGENSTRAT for genotyping analysis
Baseline transform to Median/Mean	GISTIC for CN	Genomic Control for stratification
Multiple Sample Histogram	Fawkes ASCN	Multiple and linear regression for association
Tabbed Visualization Windows	CN analysis batch correction	Haplotype Trend Regression
Genome Browser	Filter CN by known variant regions	Cochran-Armitage association test
Partial Least Squares class prediction	Find overlapping genes with CN / SNPs	Fisher's Exact association test
Identification of predictor genes		Chi-square association test
MeSH Network Builder		Tag SNP identification
		LD Plot

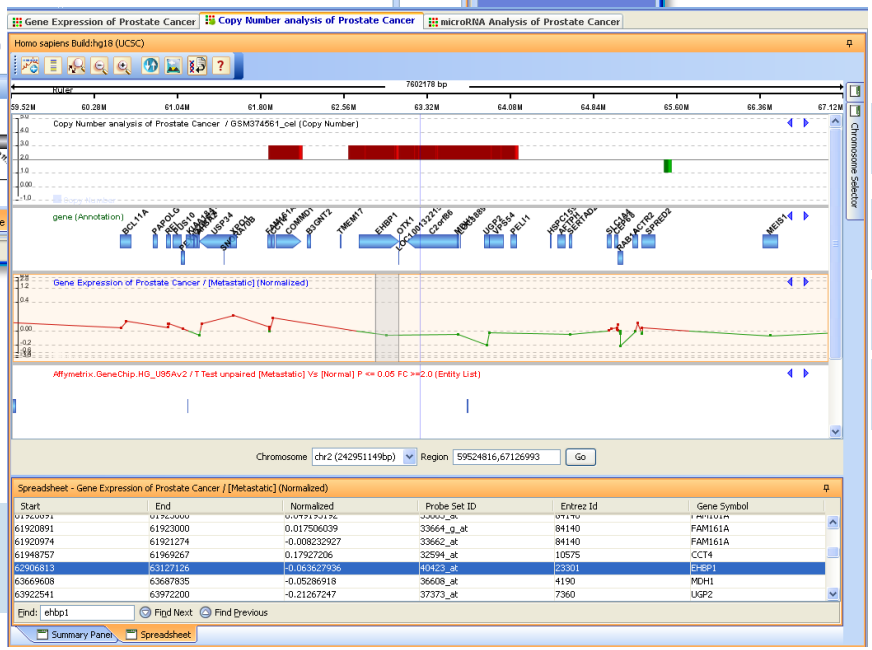
Highlights:
Genome Browser and DNA applications





Flexible and User-friendly Genome Browser





Navigation:

- Intelligent navigation by jumping to next entity of interest (Copy number region or SNP in list etc)
- Zoom in by dragging box in Chromosome Navigator or within the tracks
- Pan around region of interest
- Search for Entity of Interest by annotation (gene symbol/coordinates

Copy number data

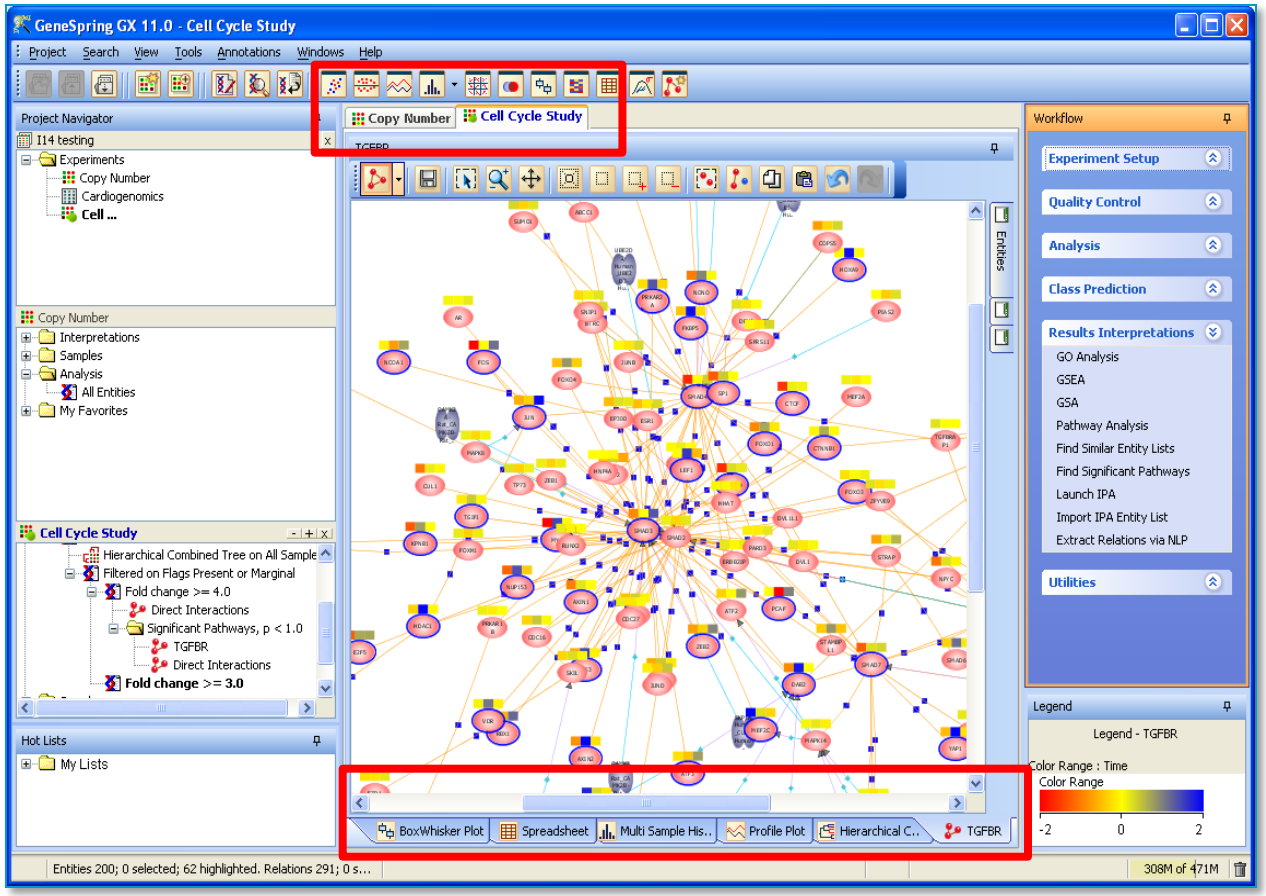
Gene track

Gene expression data

Entity List

Spreadsheet shows data for selected Track

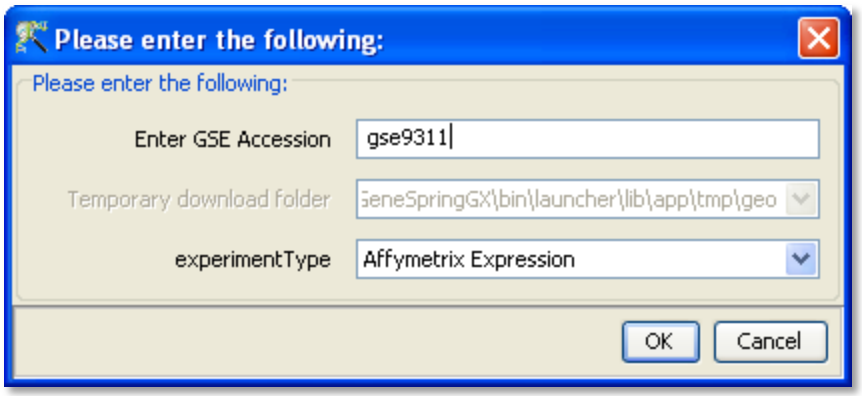
Tabbed Visualization Windows

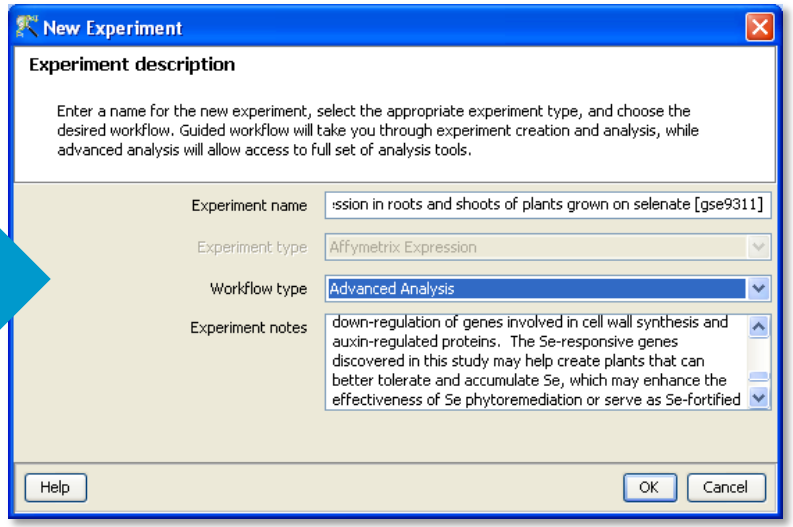


Tabbed windows allow easy switching between different visualizations and plots to facilitate interrogation and comparison of data

GeneSpring Analysis

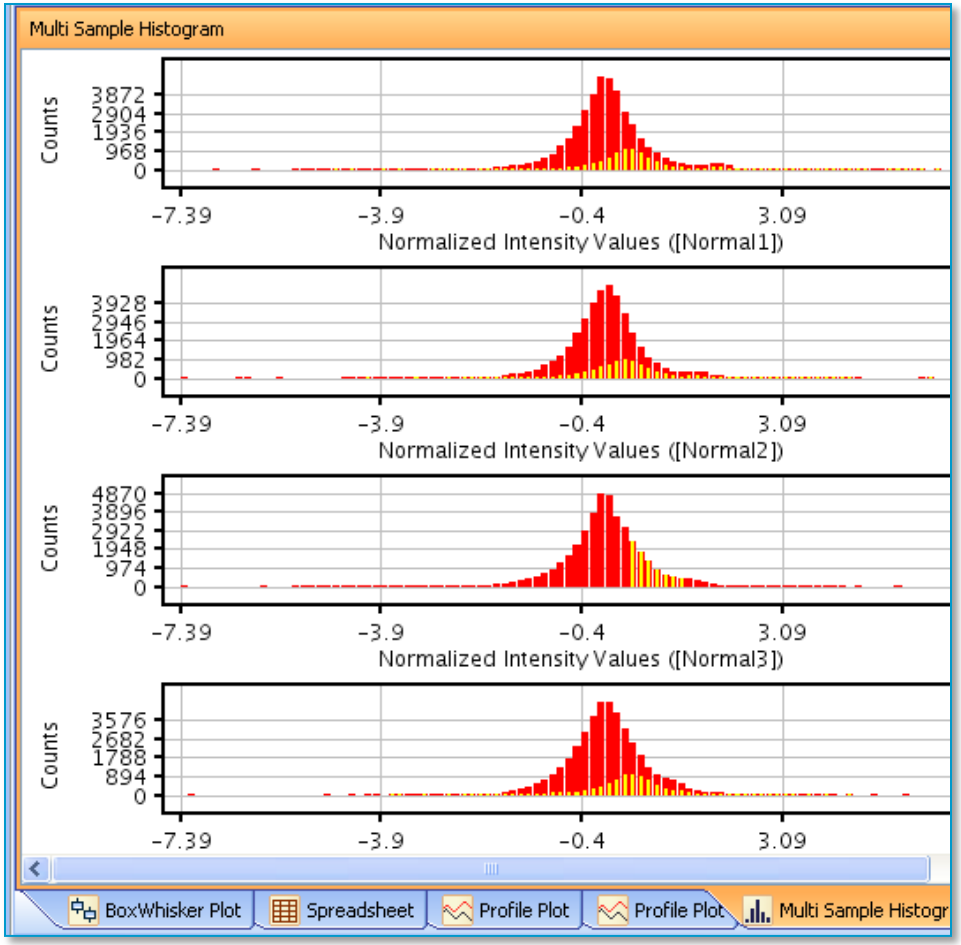
Import GEO Datasets and Create Experiments





GeneSpring Analysis - Normalization

Display Multiple Histograms in One View



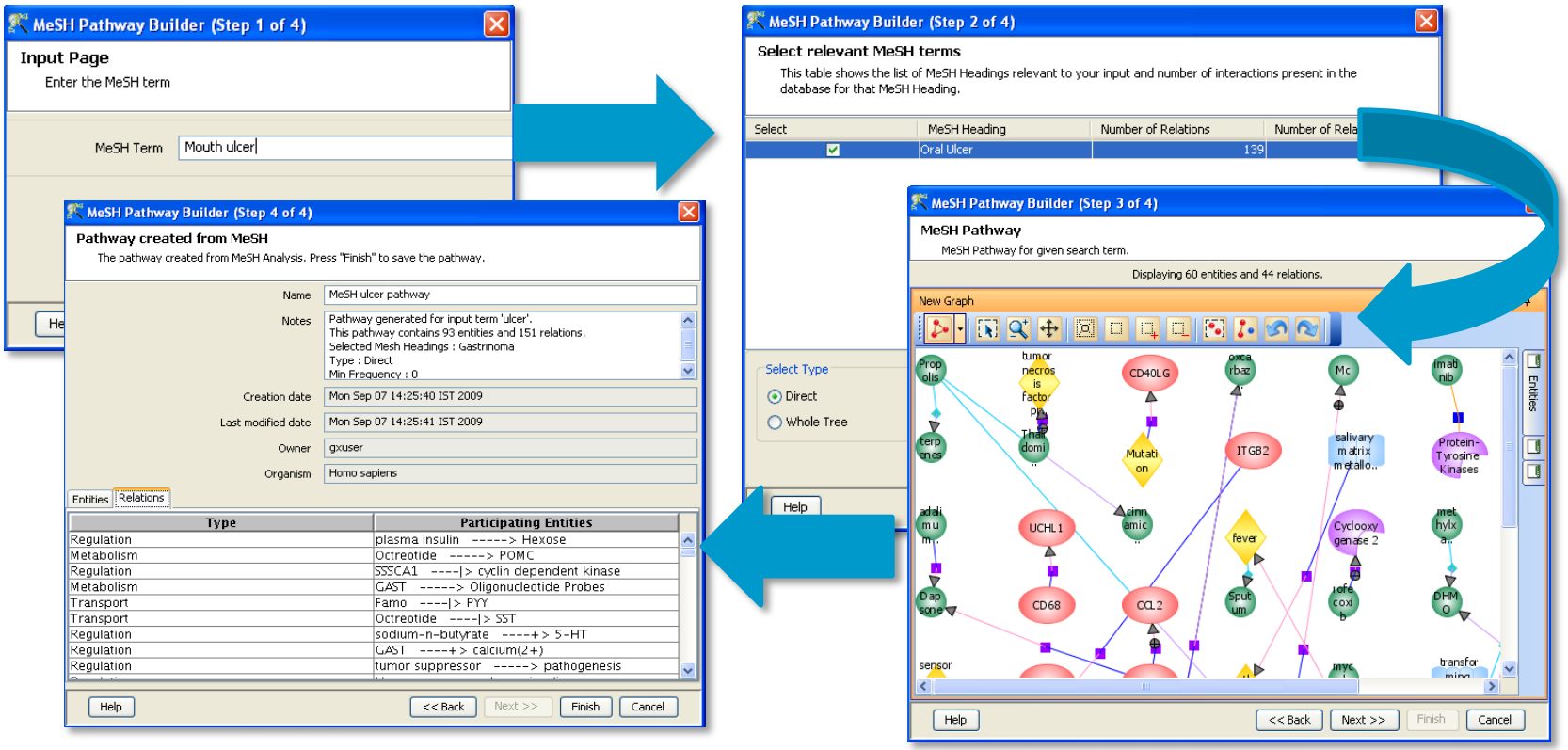
Compare distributions of intensity values across multiple samples or conditions

Plot Raw or Normalized values to assess effect of normalization

Selected Entities (yellow) are displayed across all histogram

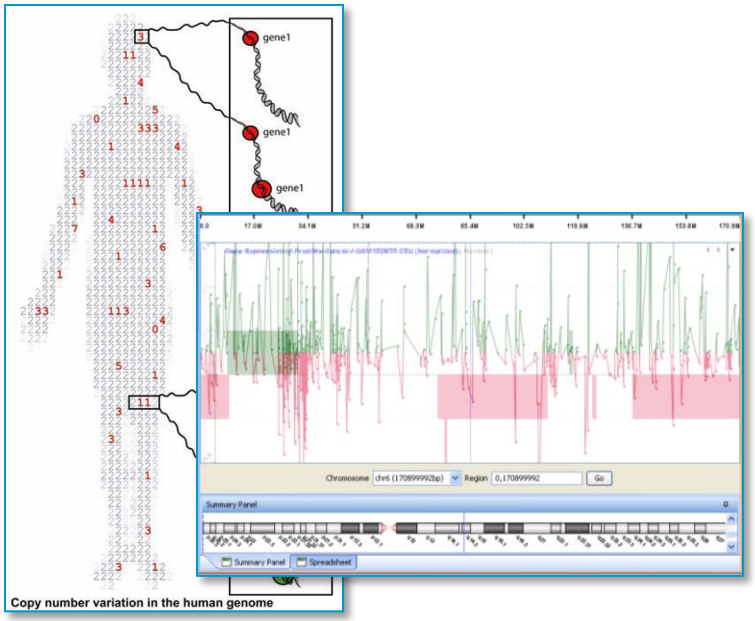
GeneSpring Analysis

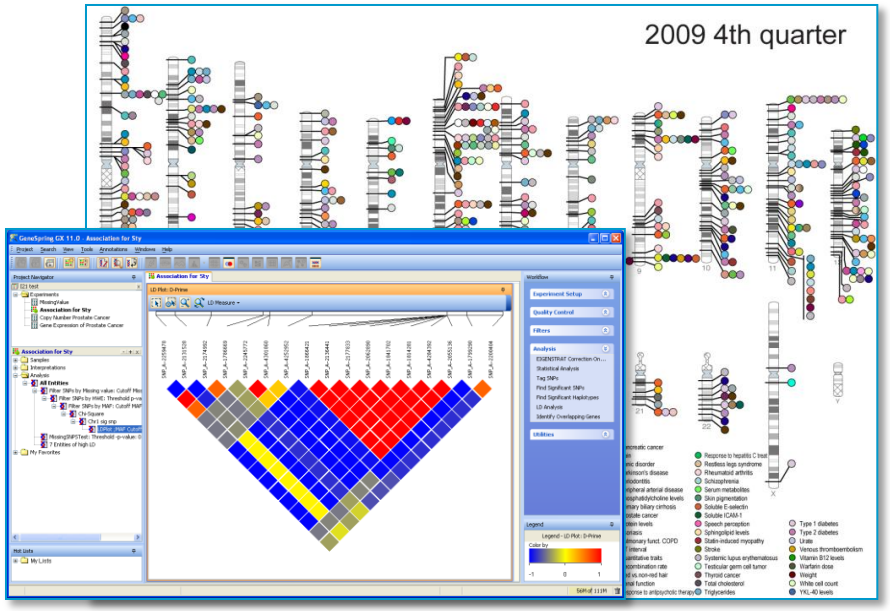
Build Networks Using Medical Subject Heading (MeSH) Terms



- Relations in Pathway Interaction databases are associated with MeSH terms
- Using MeSH term as input, retrieve relations in interaction database and build network using these relations
- This allows you to generate a network that represents molecular interactions associated with the medical concept

DNA Applications in GeneSpring GX11: CNV and GWAS analysis





Support for Affymetrix and Illumina whole-genome genotyping and CNV analysis microarrays

For CNV, Support for paired-normal and reference (standard HapMap or Custom) designs

Agilent Technologies

Support for genome-wide association studies

Supported array technologies

Affymetrix

- 100K (50K Xba, 50K Hind)*
- 500K (250K Nsp, 250K Sty)
- SNP 5.0
- SNP 6.0
- Technology available from server

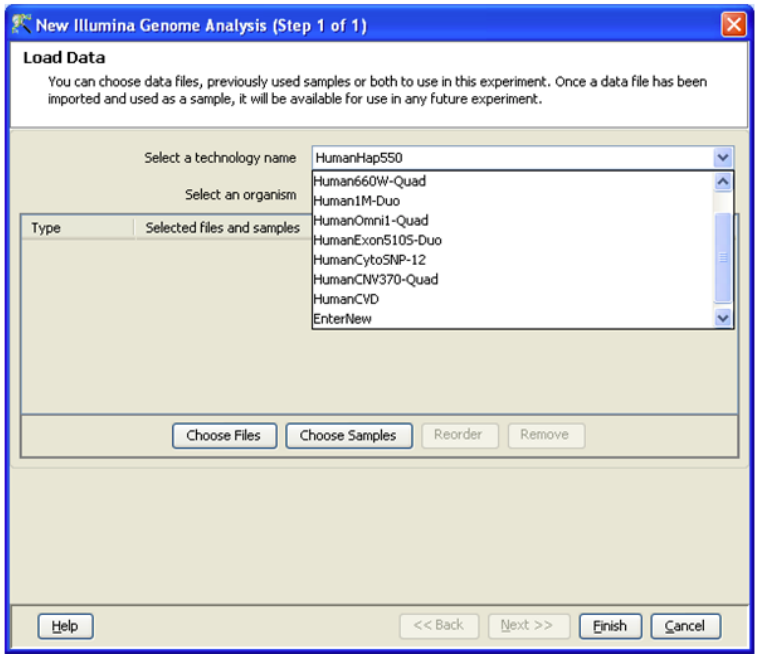
**You need at least 6 distinct cel files for Hind or Xba experiments, and 6 file pairs for combined experiments*

Illumina

- All SNP arrays
- GeneSpring GX plugin for GenomeStudio must be used to export data in the correct format

Custom

- Illumina format file input – these could be genotype calls from any other source



- Technology created during experiment creation

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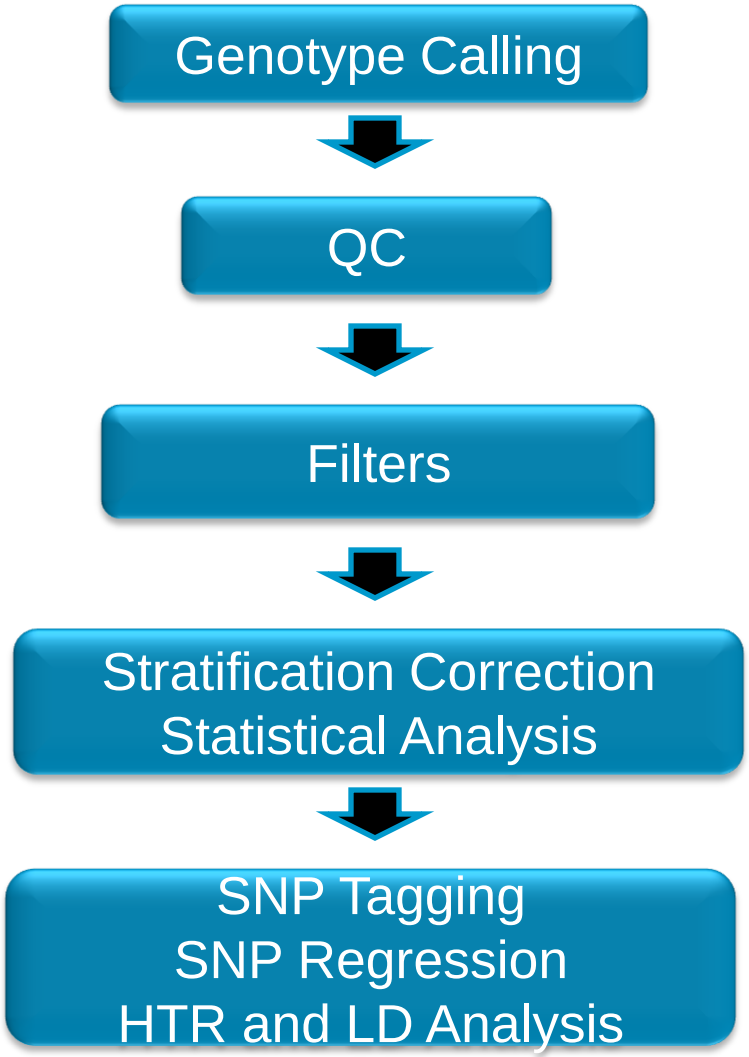
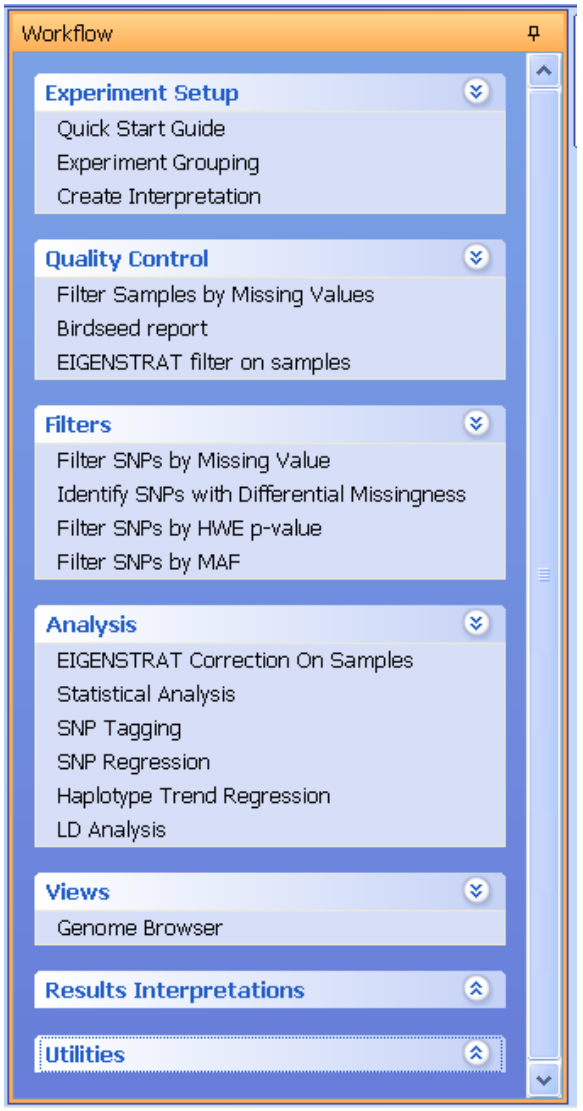
Genome-wide association studies

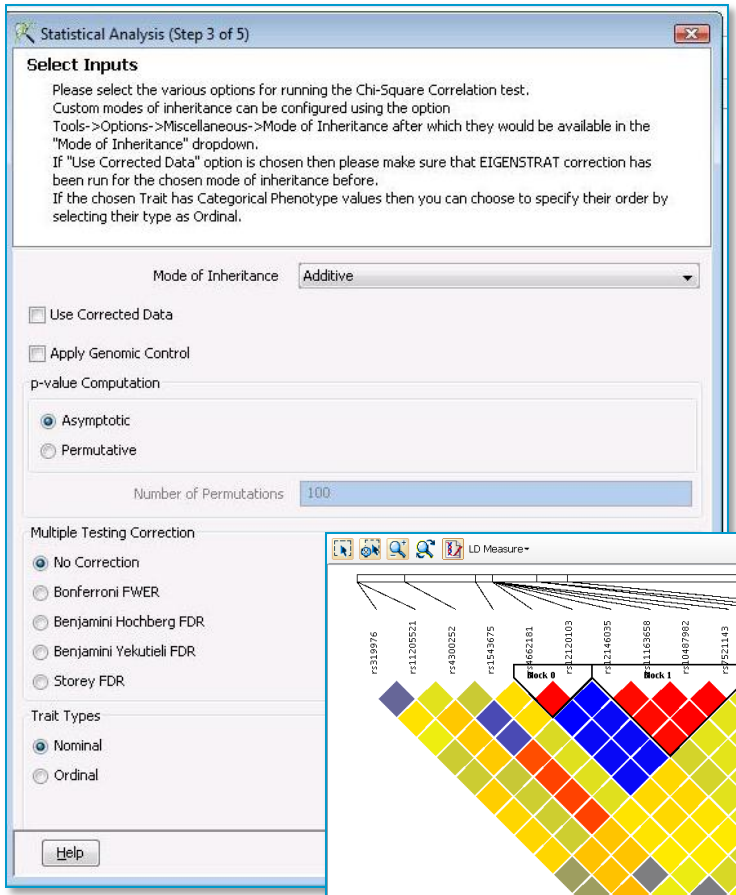
Workflow in GeneSpring GX

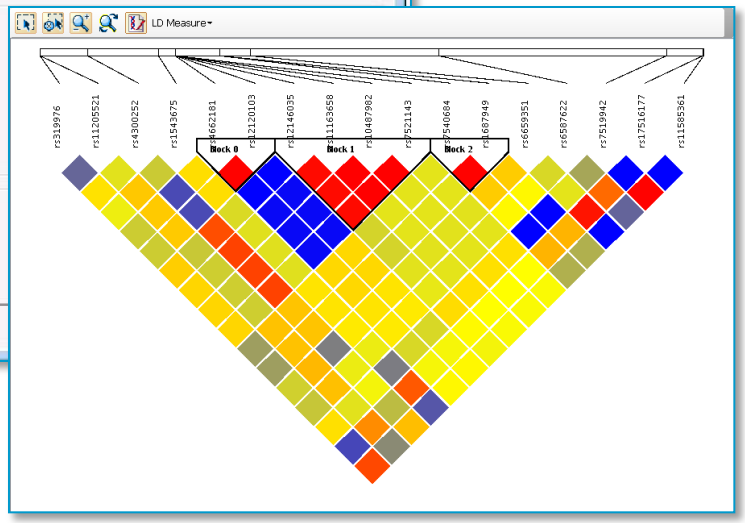




GeneSpring Analysis

Test for Association in GWAS Analysis and Linkage Disequilibrium





- Which SNPs are associated with expression of the phenotype being studied?
- 4 tests can be applied:
- Cochran-Armitage, Chi-square, Fisher's Exact and Correlation Trend for testing Individual SNPs
  - Specify models of inheritance: Additive, Dominant, Recessive, Custom

Visualize LD as R^2 or D'

Select SNPs with high LD in view and save as Entity List

Copy Number Analysis in GeneSpring GX 11

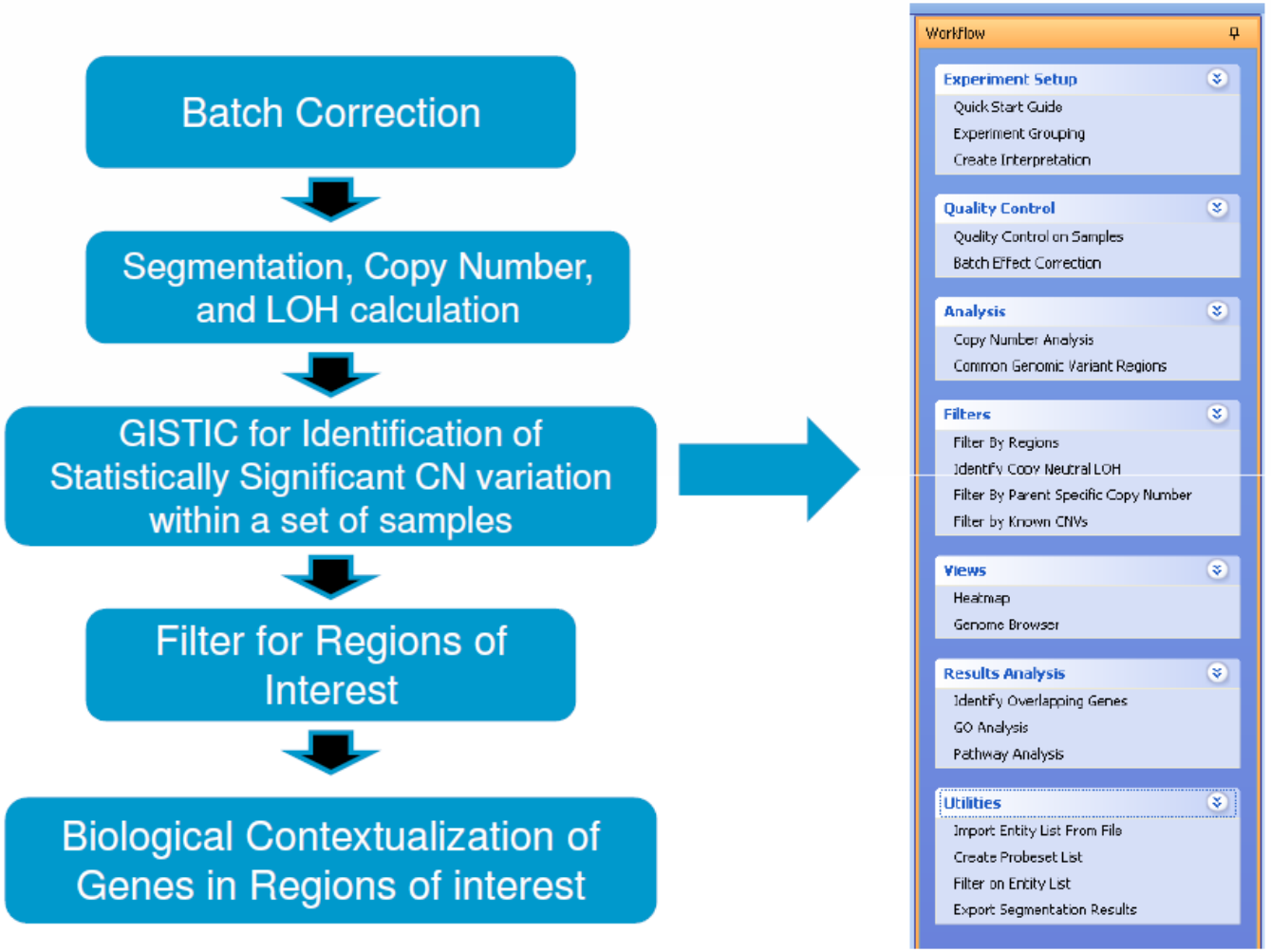
Support for Affymetrix and Illumina whole-genome genotyping and CNV analysis microarrays

Support for paired-normal and reference (standard HapMap or Custom) designs

Algorithms Used in GeneSpring:

- Affymetrix:
  - Birdseed or BRLMM for generation genotype calls
  - Circular Binary Segmentation for identification of genomic segments of equal copy number
  - HMM for calculation of LOH scores
  - Fawkes for computation of allele-specific copy number
- Illumina:
  - Import genotype calls, copy number and LOH scores from Illumina BeadStudio

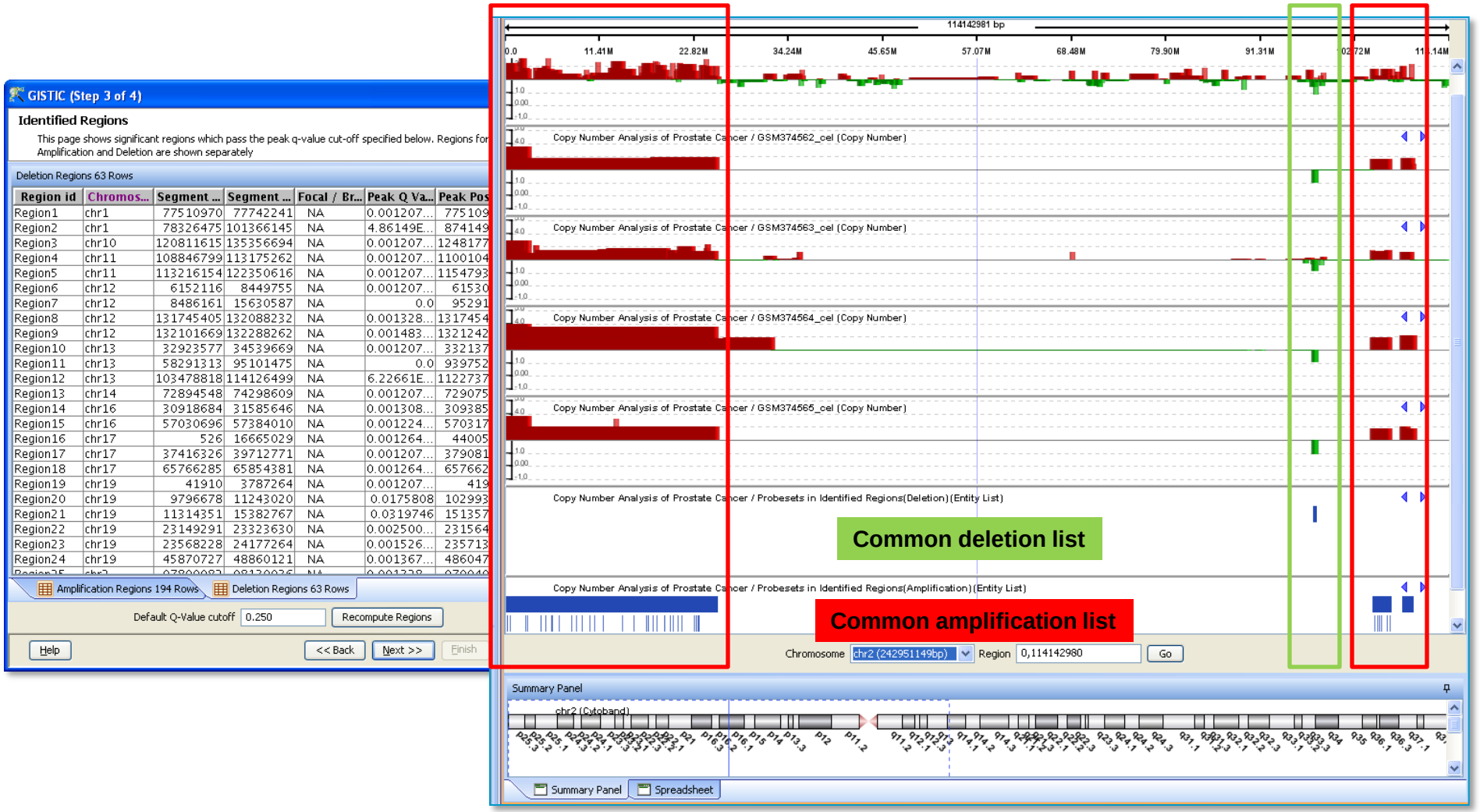
Copy Number Analysis Workflow in GeneSpring GX 11



Agilent Technologies

GeneSpring Analysis

Find Common Aberrations in CN Analysis



Joint and Multi-Omic Analysis & Biological Contextualization in GeneSpring

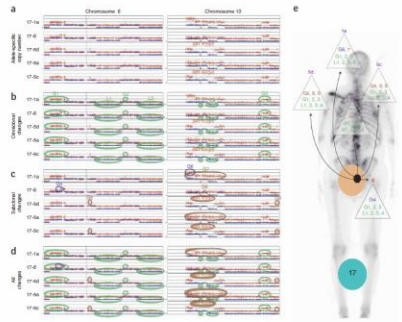
Joint Analysis of Gene Expression and Genomic Copy Number Data in Metastatic Prostate Cancer

Copy Number Analysis in Prostate Cancer Samples

nature medicine

Copy number analysis indicates monoclonal origin of lethal metastatic prostate cancer

Wennuan Liu[1,9], Sari Laitinen[2,9], Sofia Khan[3], Mauno Vihinen[3], Jeanne Kowalski[4], Guoqiang Yu[5], Li Chen[5], Charles M Ewing[6], Mario A Eisenberger[7], Michael A Carducci[7], William G Nelson[7], Srinivasan Yegnasubramanian[7], Jun Luo[6,7], Yue Wang[5], Jianfeng Xu[1], William B Isaacs[6,7], Tapio Visakorpi[2] & G Steven Bova[6–8]



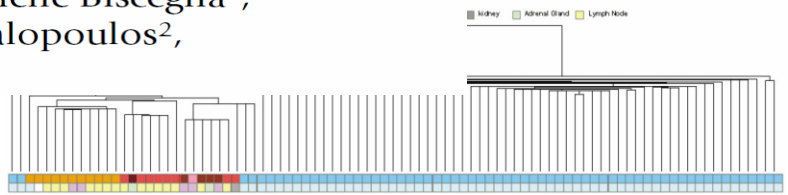
Expression Analysis in Prostate Cancer Samples

BMC Cancer

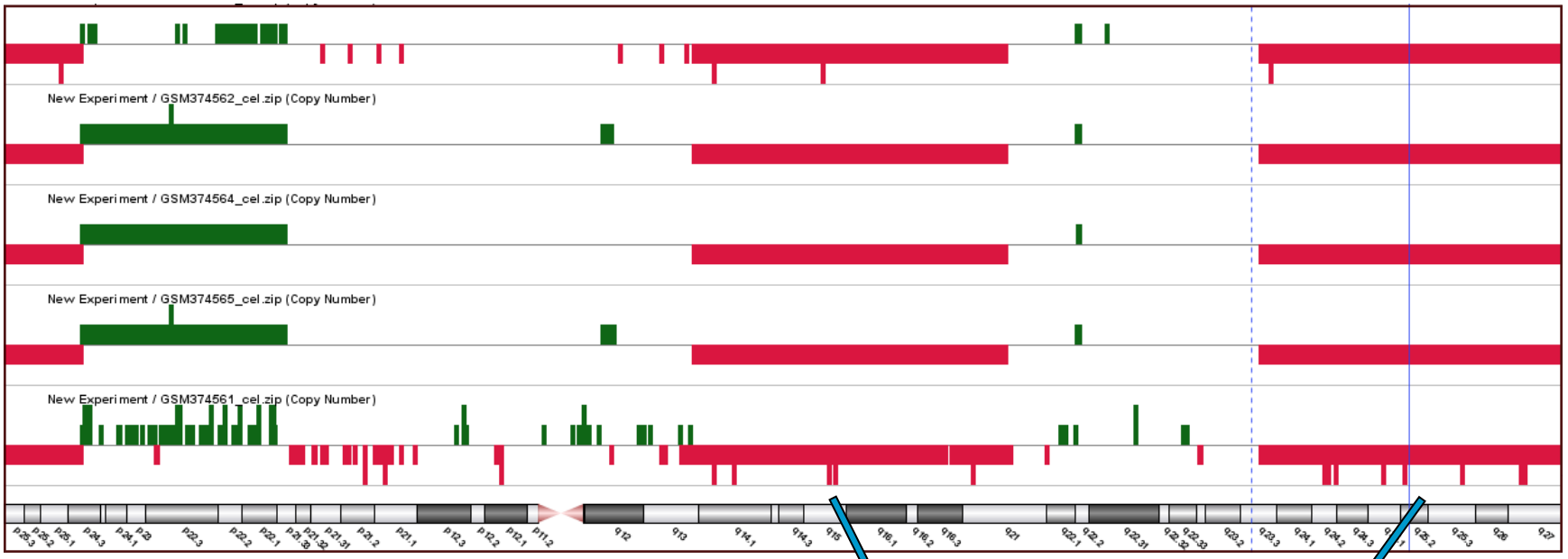
Research article

Gene expression profiles of prostate cancer reveal involvement of multiple molecular pathways in the metastatic process

Uma R Chandran*[1], Changqing Ma[2], Rajiv Dhir[2], Michelle Bisceglia[2], Maureen Lyons-Weiler[2], Wenjing Liang[2], George Michalopoulos[2], Michael Becich[1,2] and Federico A Monzon[2]



Deletion in q-arm of Chr 6 Detected in all Five Metastatic Locations of Patient #17

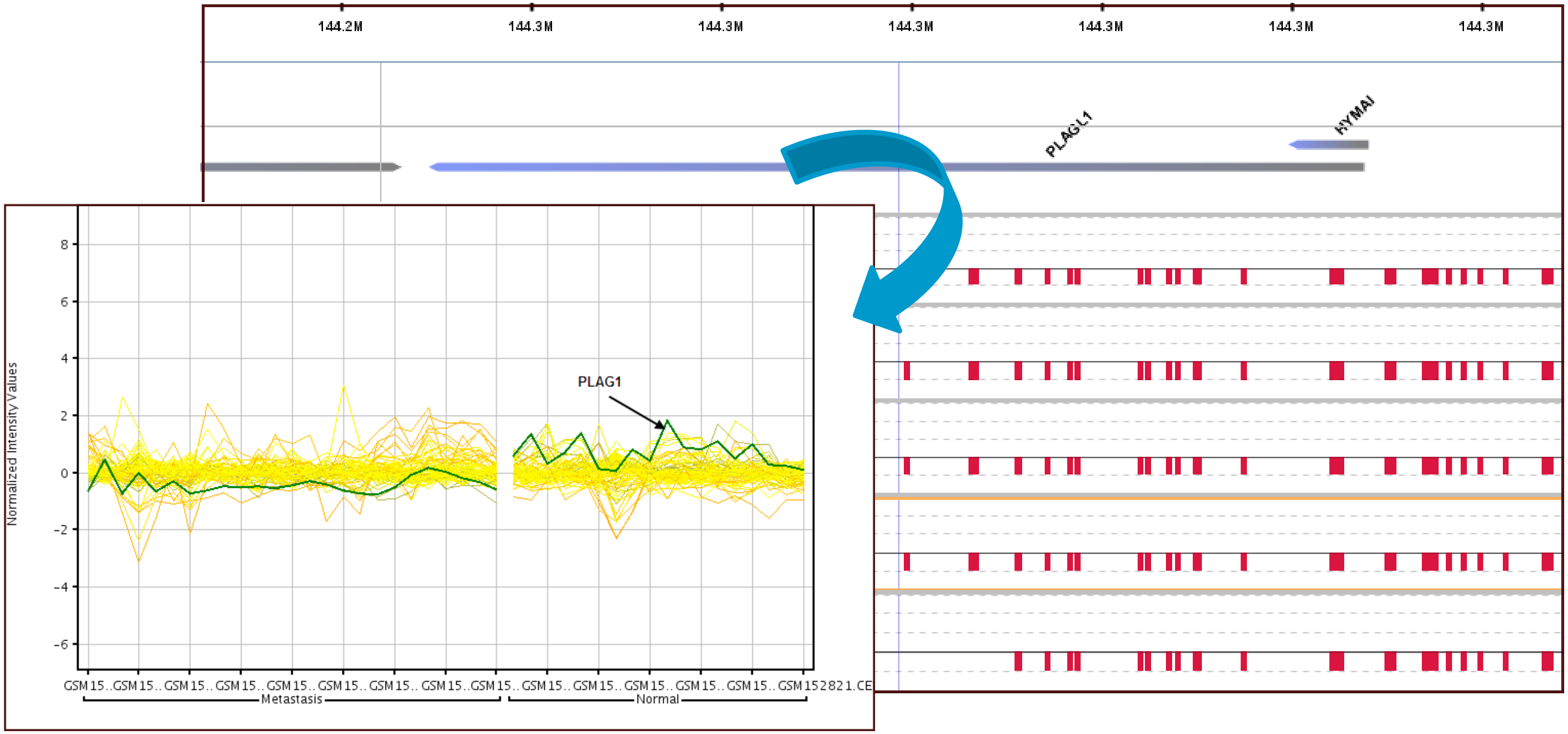


p-arm region amplification

Deletion of 2 large regions across the q-arm observed in all 5 metastatic locations in 1/14 patients

GeneSpring Analysis

Finding Overlapping Genes and Functional Groupings



- In a prostate cancer study, deleted Chr 6 q-arm regions contains enrichment of genes involved in immune response and antigen processing and presentation
- All 5 metastatic tumors from this patient were found in lymph nodes
- PLAGL1 is significantly down-regulated in metastatic prostate cancer

PLAGL1 Gene

- No previous association to prostate cancer reported
- Frequently deleted in many solid tumors such as breast, ovarian, and renal cell carcinomas

- Biological properties:
  - Zinc finger protein with transactivation and DNA binding activity
  - Candidate tumor suppressor gene with anti-proliferative activities

GeneSpring 11 Press Release

GEN Genetic Engineering & Biotechnology News

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Microarrays Breaking News

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Dec 7 2009, 11:00 AM EST

TRADE NEWS: Agilent Technologies Adds Genetic Association and Copy Number Variation Analyses to Bioinformatics Software, Expanding Systems Biology Suite

News source: **Business Wire**

Agilent Technologies, Inc. (NYSE:A) introduced GeneSpring GX 11, the latest generation of its popular desktop software for visualizing and analyzing microarray data, and GeneSpring Workgroup 11, the enterprise version of the GeneSpring desktop software.

Designed to support multi-omics research, GeneSpring 11 adds capabilities for genetic association analysis using genotyping data, genomic copy number analysis, and other analytical and visualization tools to facilitate comparison of these heterogeneous data. Agilent's bioinformatics portfolio also includes Mass Profiler Professional, built on the same platform as GeneSpring, supporting proteomics and metabolomics data analysis.

"The multi-omics approach to defining mechanism of disease in systems biology research has created a bioinformatics bottleneck, where the ability to extract biological knowledge from the data often lags behind the ability to generate the data," said Chris Grimley, Agilent senior director of marketing, Genomics. "GeneSpring 11 was developed with this bottleneck in mind and addresses some of the challenges of integrative analysis."

"GeneSpring 11 represents a significant advance in data analysis software for life sciences," said Bruce Aronow, Ph.D, scientific director of the Center for Computational Medicine at Cincinnati Children's Hospital Medical Center, and a longtime GeneSpring user. "Here we see for the first time an all-wheel driving machine for multi-omics technologies that shape a new roadmap for integrative systems biology."

In GeneSpring 11, researchers can have multiple experiment types, such as microRNA, gene expression, genotyping, and copy number, open simultaneously within a single window. This allows users to move back and forth between the data as needed without having to load each experiment separately. This functionality also allows researchers to easily combine data within a logical unit and compare results from different experiment types.

GeneSpring 11 also allows researchers to find critical linkages and concordance between them.

While there are other software applications that support multi-omics data analysis, a major differentiator of GeneSpring 11 is the ease with which users can compare

DYNAMIC REPORTS. DYNAMIC CONTENT. DYNAMIC SCIENCE.

Done

Customer quote:

Bruce Aronow
Director of the Center for Computational Medicine
Cincinnati Children's Hospital

"GeneSpring 11 represents a significant advance in data analysis software for life sciences. Here we see for the first time an all-wheel driving machine for multi-omics technologies that shape a new roadmap for integrative systems biology."

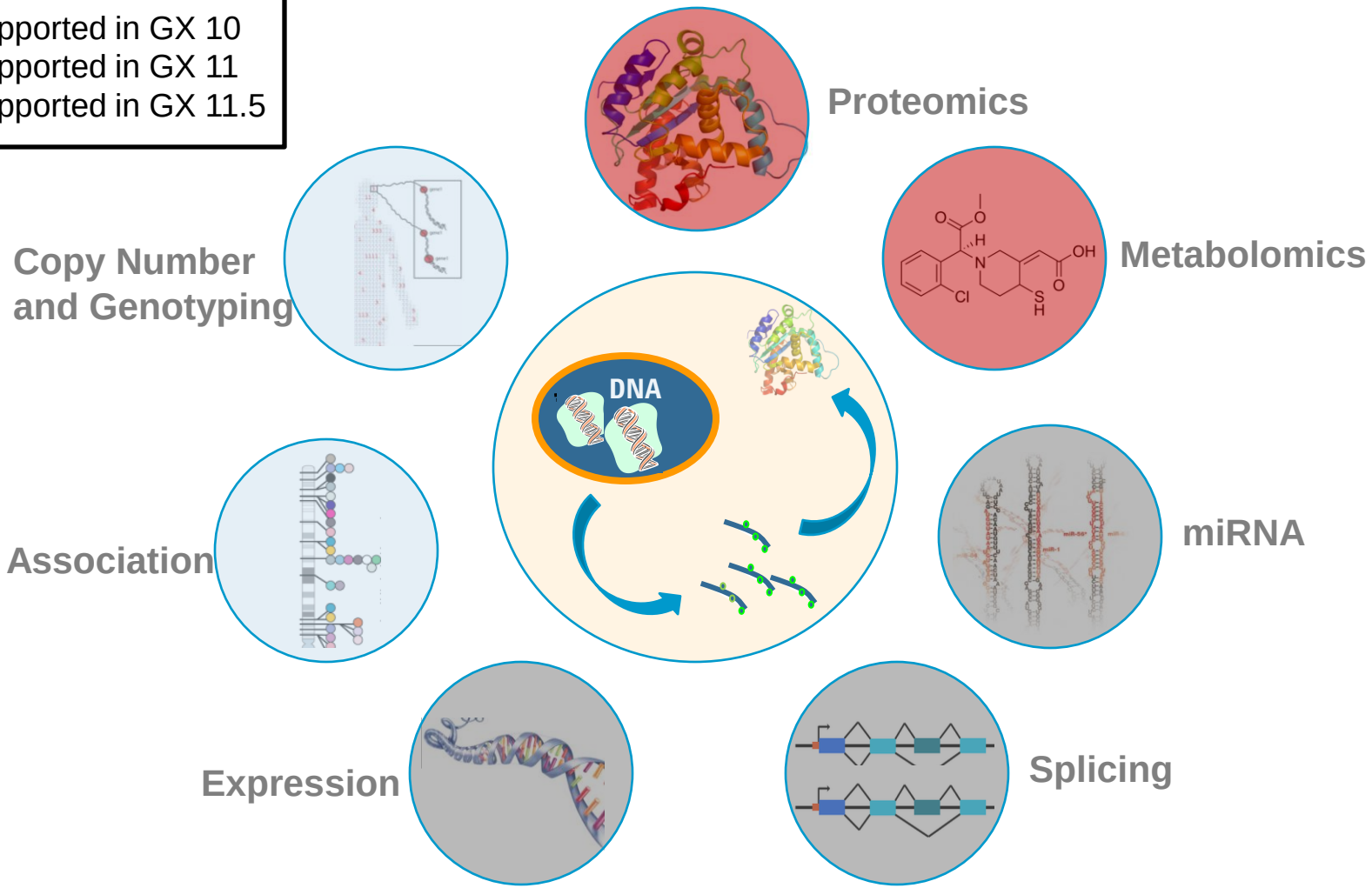
Where we are going: GeneSpring 11.5

2010:

- -Integrative Biology
  - -Integrated Mass Profiler Pro into GX 11
- -Support for Agilent Exon Arrays
- -MetaCore Integration
- -Useability Enhancements

Systems Level Research Leads to a More Complete Understanding of Biological Processes

- Supported in GX 10
- Supported in GX 11
- Supported in GX 11.5



Systems Level Research Leads to a More Complete Understanding of Biological Processes

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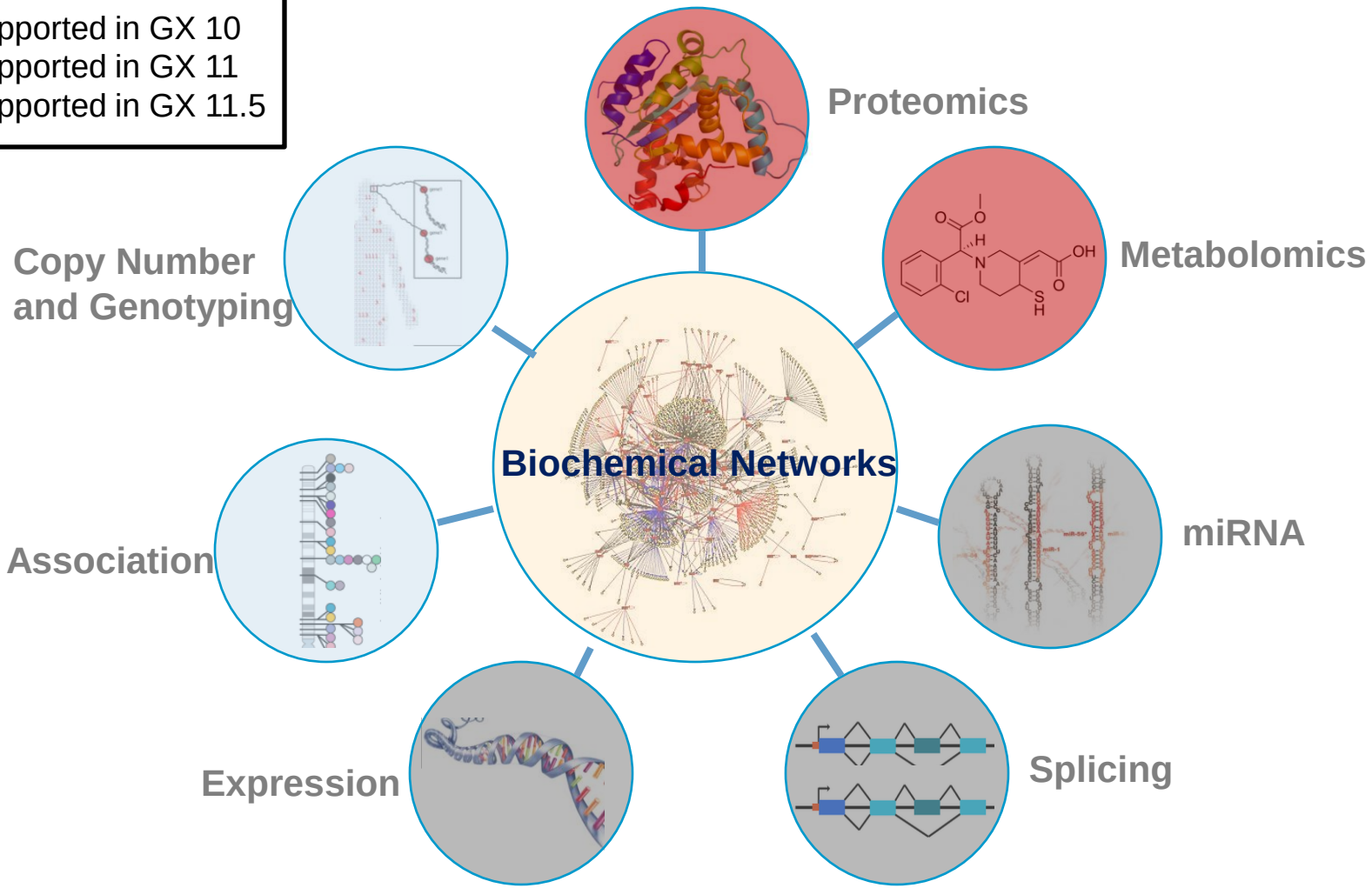


A Case for Multi-Omics Data Analysis

Cross-Technology Panels for Biomarker Research

Gene Symbol	Gene	Gene Symbol	Protein
CHPT1	choline phosphotransferase 1	IGFBP3	insulin-like growth factor binding protein 3 isoform a precursor
RPS26	ribosomal protein S26	MST1	Hepatocyte growth factor-like protein precursor
GBP3	guanylate binding protein 3	CFHR1	Complement factor H-related protein 1 precursor
KLRC1	killer cell lectin-like receptor subfamily C, member 1	CPN1	Carboxypeptidase N catalytic chain precursor
ZCCHC2	zinc finger, CCHC domain containing 2	CDH5	Cadherin-5 precursor
IFIT5	interferon-induced protein with tetratricopeptide repeats 5	APOB	Apolipoprotein B-100 precursor
CLEC2B	C-type lectin domain family 2, member B	HBB	Hemoglobin subunit beta
PDK4	pyruvate dehydrogenase kinase, isozyme 4	C1QB	Complement component 1, q subcomponent, B chain
OSBP2	oxysterol binding protein 2	GC	Vitamin D-binding protein precursor
(242907_at)	Homo sapiens mRNA; cDNA DKFZp451C2311	C9	Complement component C9 precursor

No overlap between 10 genes and 10 proteins for Cardiac Allograph Vasculopathy (CAV)

- Gene-ontology-based analyses revealed a great degree of biological concordance
- Cross-technology panels often outperform corresponding single platform panels

•Long-term survival of cardiac transplant recipients is still a major hurdle
•Cardiac allograft vasculopathy (CAV) is an expression of chronic rejection
•Current standard diagnosis of CAV is expensive and invasive (agiography and intravascular ultrasound)
•Aim is to derive a non-invasive biomarker panel based on whole blood mRNA and plasma proteins

Mass Spectometry Module to GeneSpring GX

Mass Spectometry Module to GeneSpring GX has all features of MPP plus…

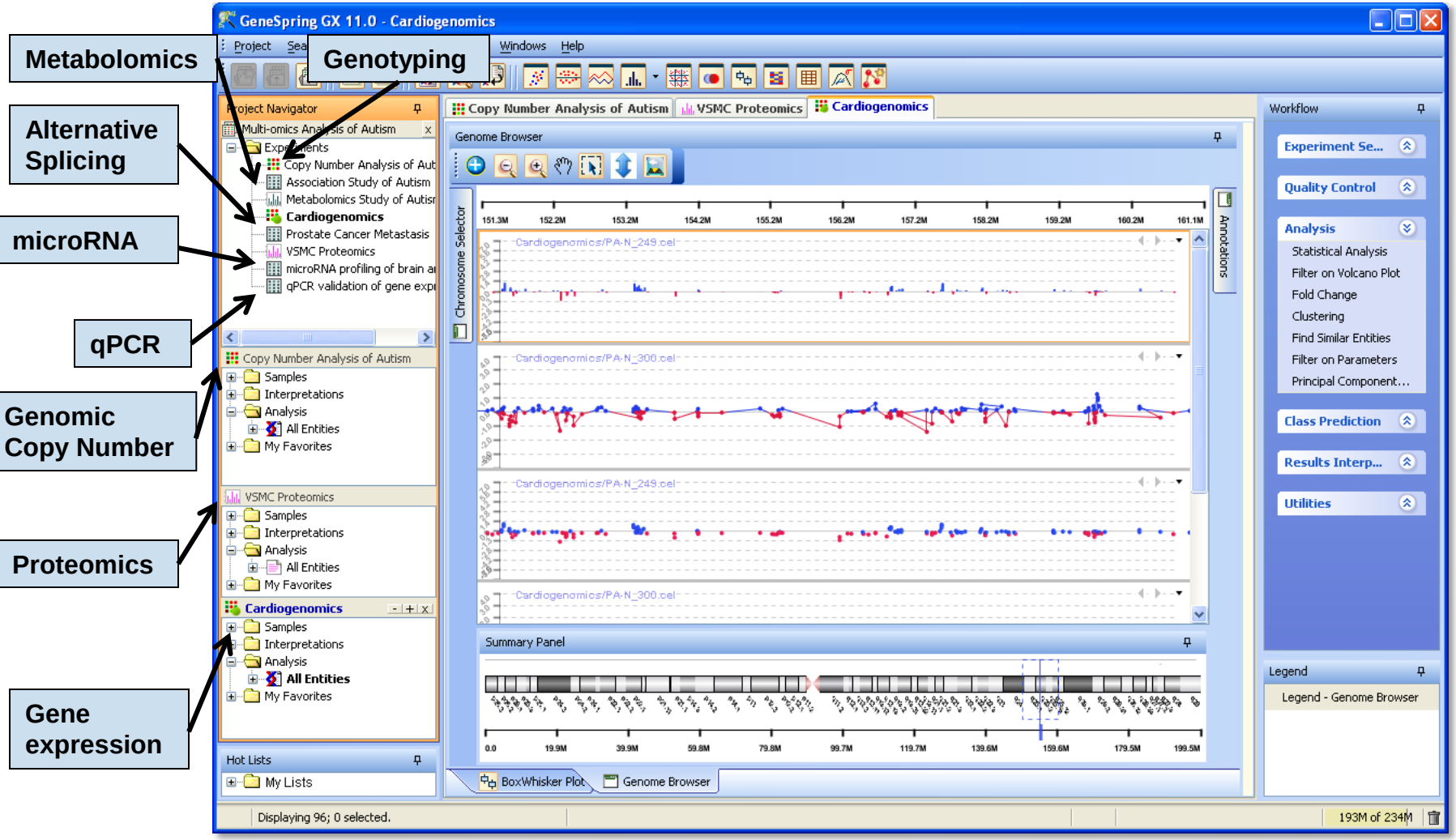
- Client-server analysis environment (through connection to Workgroup) in addition to desktop
- Ability to combine mass spec experiments with genomics experiments in a GeneSpring Project

Expected availability date for module- Summer 2010

Module can be purchased as an add-on module to GeneSpring GX

Integrated Analysis in GeneSpring 11.5

(Summer 2010)

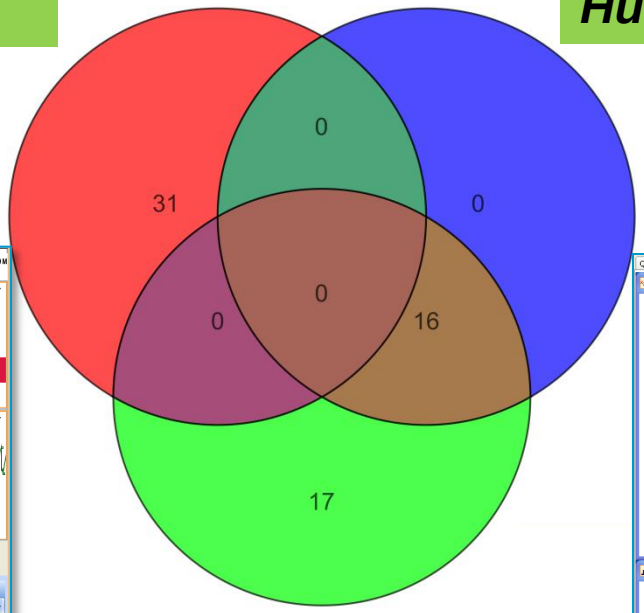


Joint and Multi-Omics Analysis

Easily Translate Between Technology Platforms, Organisms, and Data Types

Copy Number ***Affymetrix*** ***Mouse***

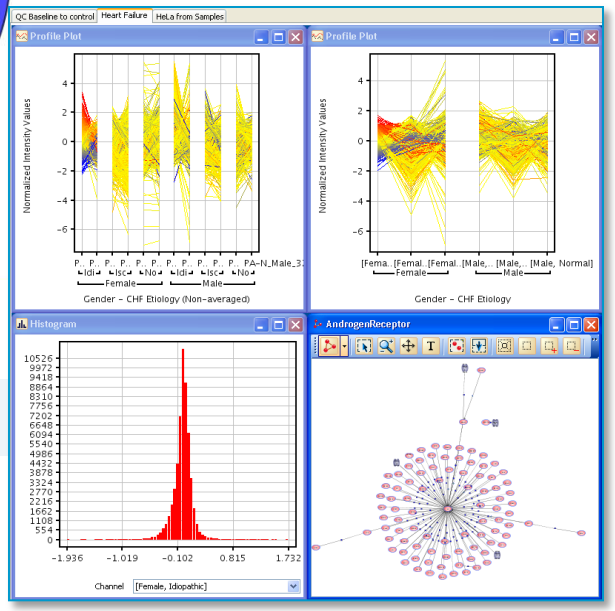
Agilent ***Gene Expression*** ***Human***



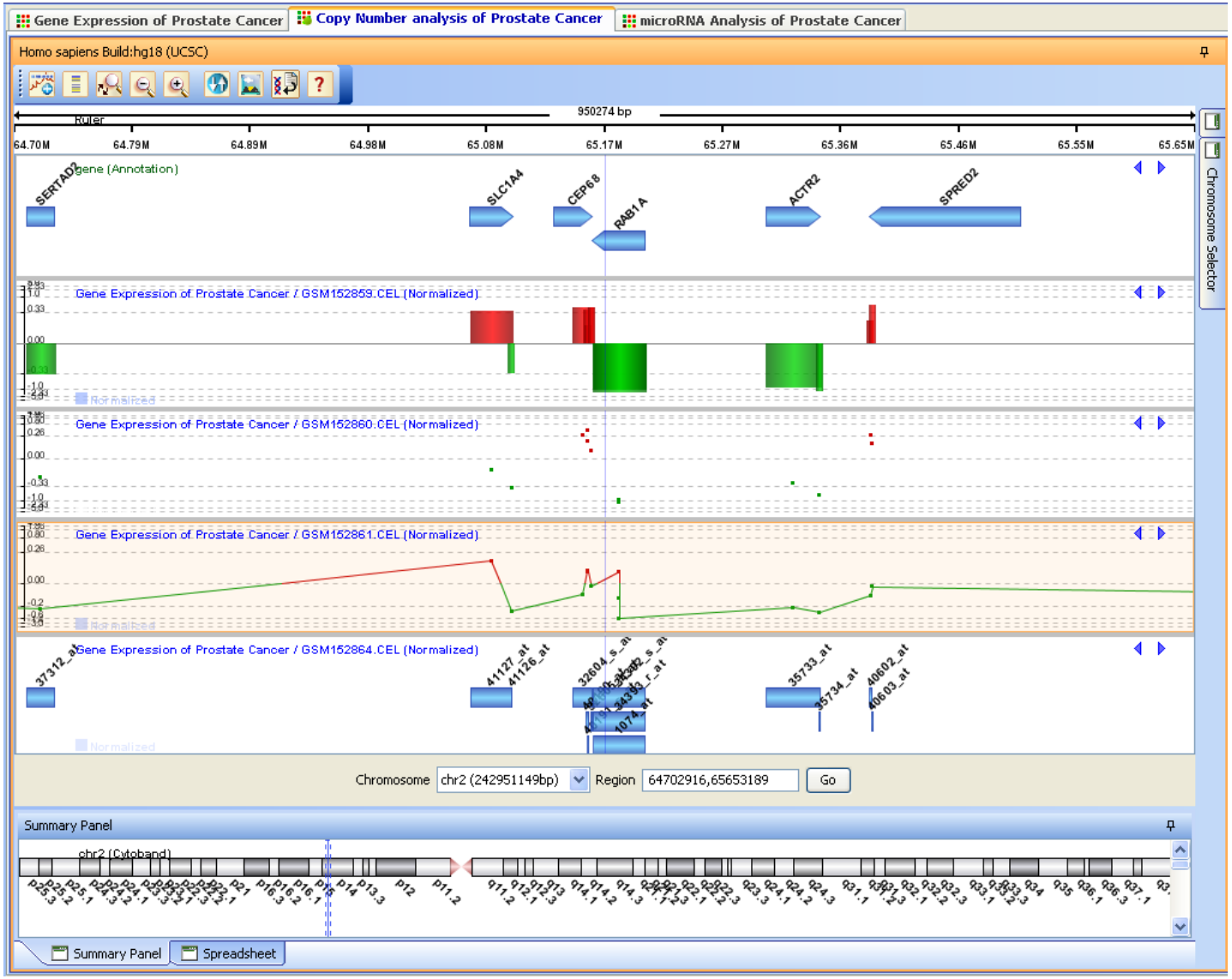
Illumina ***Genotyping*** ***Rat***

Copy Number Data

Expression Data



Positional Representation - Genome Browser



Annotation Track

Histogram

Scatter Plot

Profile Plot

Region Plot

GeneExpression
SNP
Exon
Agilent CGH/ChIP/CH3

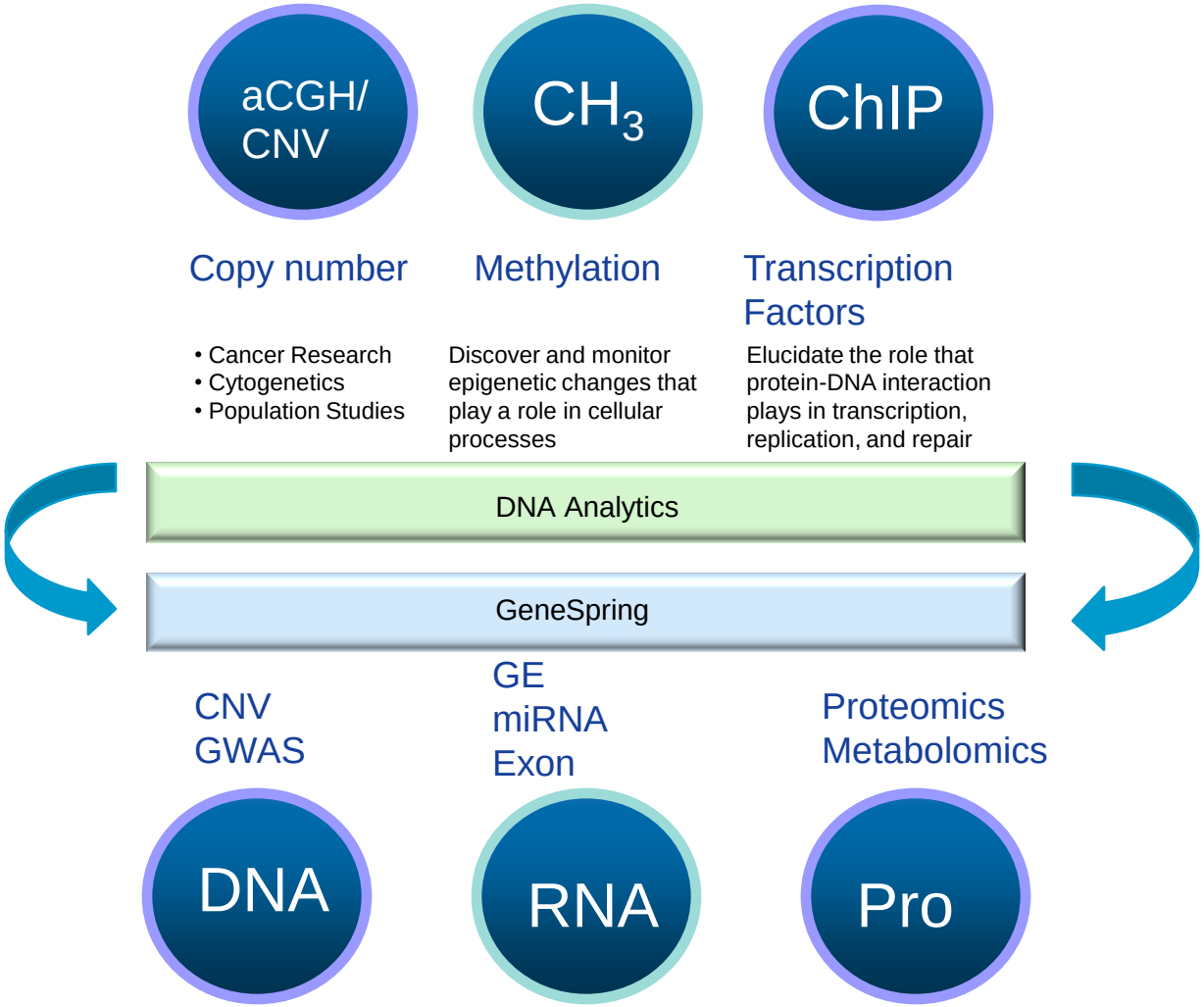
Beyond GeneSpring 11.5

2011:

-Improved Pathway Analysis (additional organisms)
-Integration with DNA Analytics
-Cytoscape connector

Agilent Genomic Workbench – DNA Analytics

Applications for Agilent Arrays

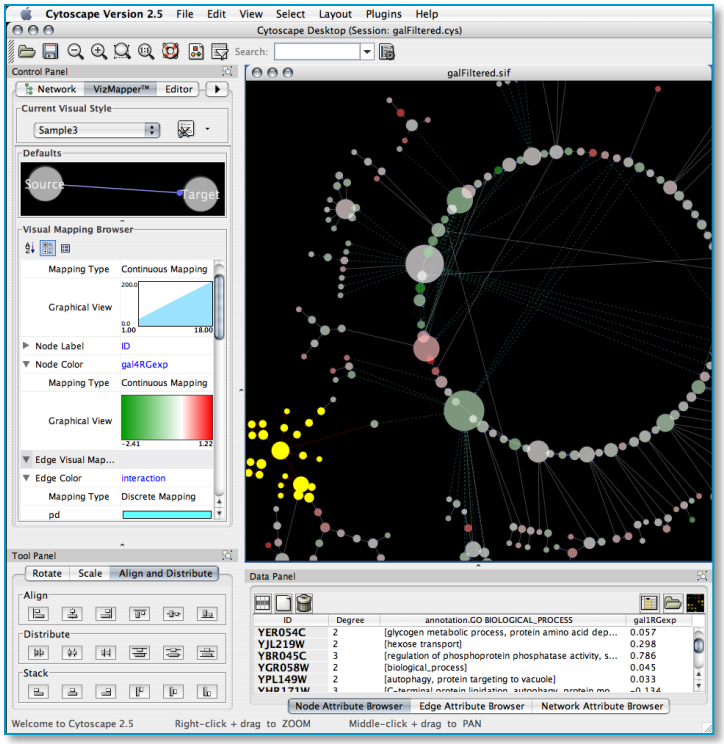


Agilent Technologies

Multi-omic Analysis

Cytoscape

Cytoscape is an open source software platform for *integrating, analyzing,* and *visualizing* measurement data in their biological context.



Cytoscape is a collaboration between

- University of California, San Diego
- Institute for Systems Biology
- Memorial Sloan-Kettering Cancer Center
- Institute Pasteur
- Agilent Technologies
- University of Toronto
- Gladstone Institute for Cardiovascular Disease
- University of California, San Francisco
- Unilever
- National Center for Integrative Biomedical Informatics

freely available at http://www.cytoscape.org

- 80000+ downloads for 2.x release; 25,000 downloads in 2007 alone; 3500/month
- Currently 100 registered plugins, developed by leading research groups, freely available
- Community development of plugins strongly encouraged and actively supported by core development team.

Web Resources at www.genespring.com

Tutorials

- Data analysis tutorials for Affymetrix gene expression, Agilent gene expression, Exon Splicing, Genomic Copy Number

Viewlets

- Short animated tutorials on various topics such as Quality Control on samples, Updating Pathway Interactions, miRNA Analysis Using TargetScan and more

Recorded and Live eSeminars

- Sign up for live eSeminars on various topics such as Introduction to GeneSpring GX 11, Joint Analysis of Gene Expression and Genomic Copy Number data, and more
- View recorded past eSeminars

GeneSpring GX Workshops

- Register for Levels I, II, and III GeneSpring GX training workshops

The GeneSpring Team

Director of Genomics Software
- Michael Rosenberg

GeneSpring Product Manager
- Michael Janis

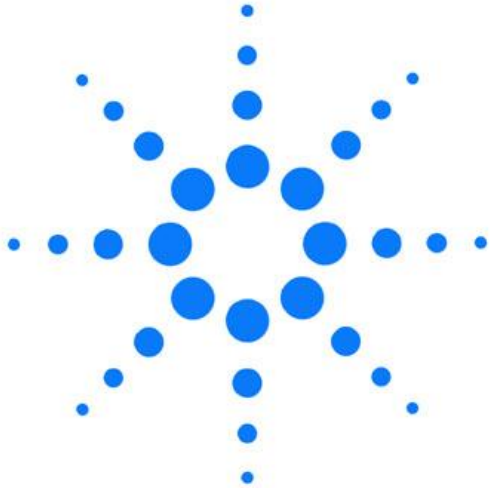
GeneSpring Project Manager
- Jayati Ghosh

Workgroup Server Product Manager
- Alexi Zubiria

Global Bioinformatics Support Manager
- Mary Jane Van Sant

GeneSpring Support
- Yosuke Konishi

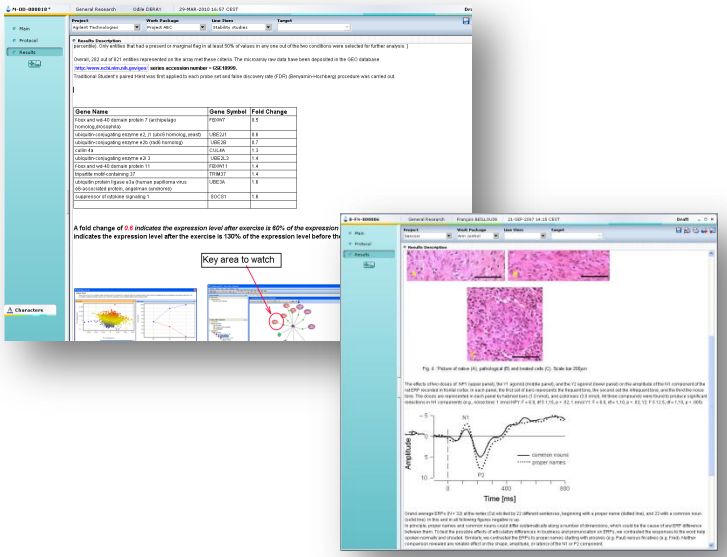
GeneSpring Product Specialist
- Antoni Wandycz



Thank you!

Bioinformatics User Group Meeting

May 12th, 2010



OpenLAB
UNLOCKS YOUR
LAB'S POTENTIAL

Have you ever tried to find…

the one buffer recipe that produced the best assay results to use today?

From chaos…

to a single search in seconds…

OpenLAB: Integrated Informatics Portfolio

Discovery databases

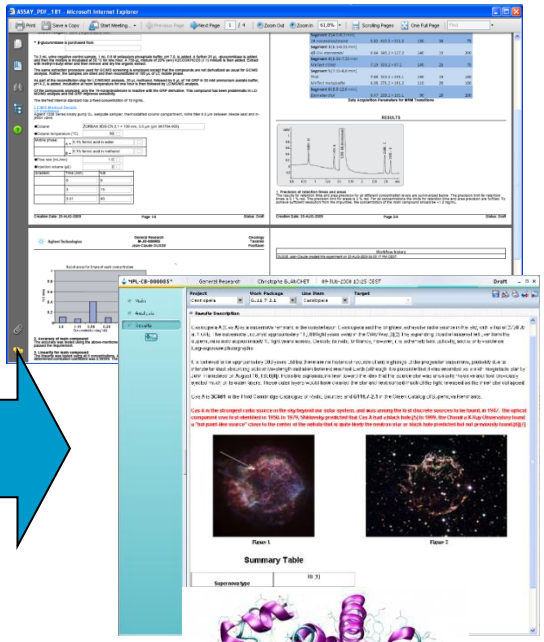
Reporting

LIMS

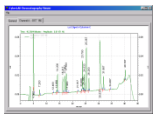
OpenLAB Electronic Laboratory Notebook

OpenLAB Enterprise Content Management System

Automatic Data Capture

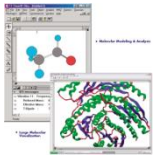


Instruments

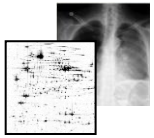


Legacy Data

MS Office



Drawings



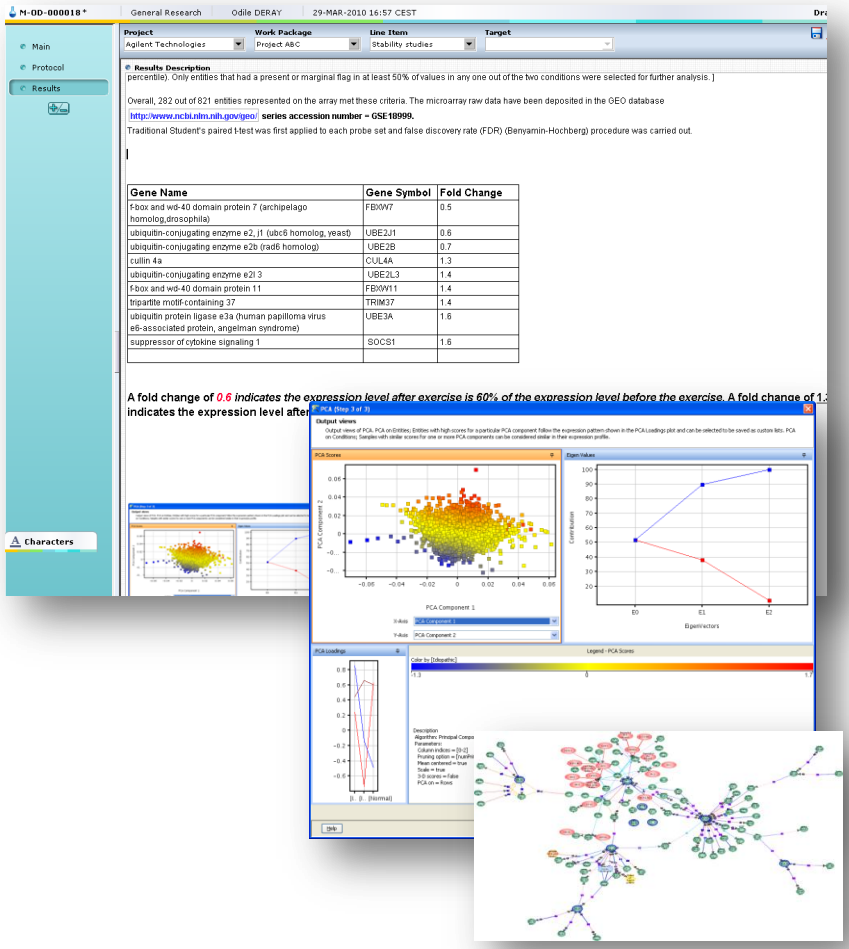
Images

Content

OpenLAB ELN for Genomics

A Web-based ELN which enables you to…

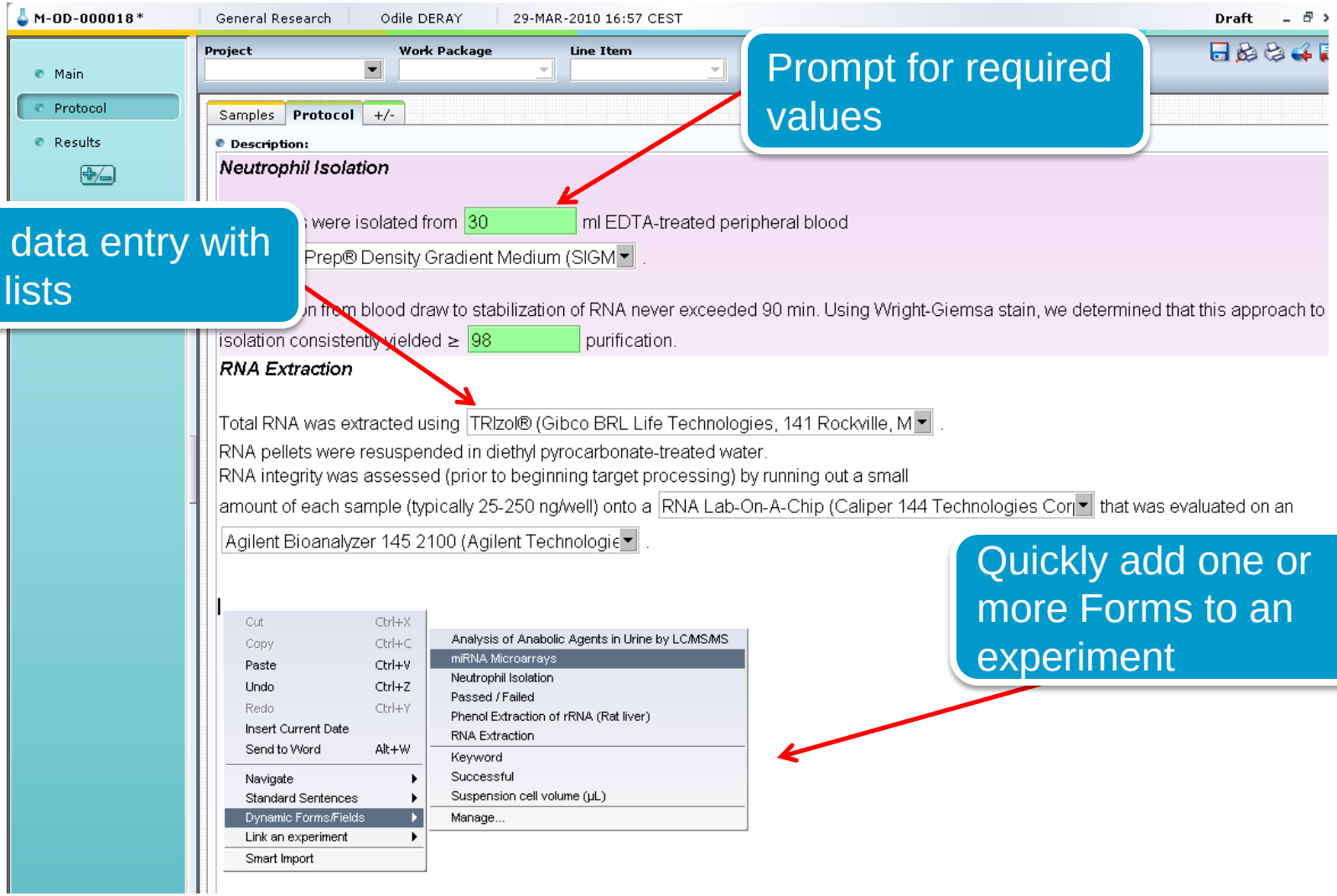
- Document, manage and analyze research across multiple disciplines
- Search and collate disparate data sources into single experiment with high level of traceability
- Reduce cycle times with integrated workflow processing to improve lab efficiency
- Integrate with existing information systems



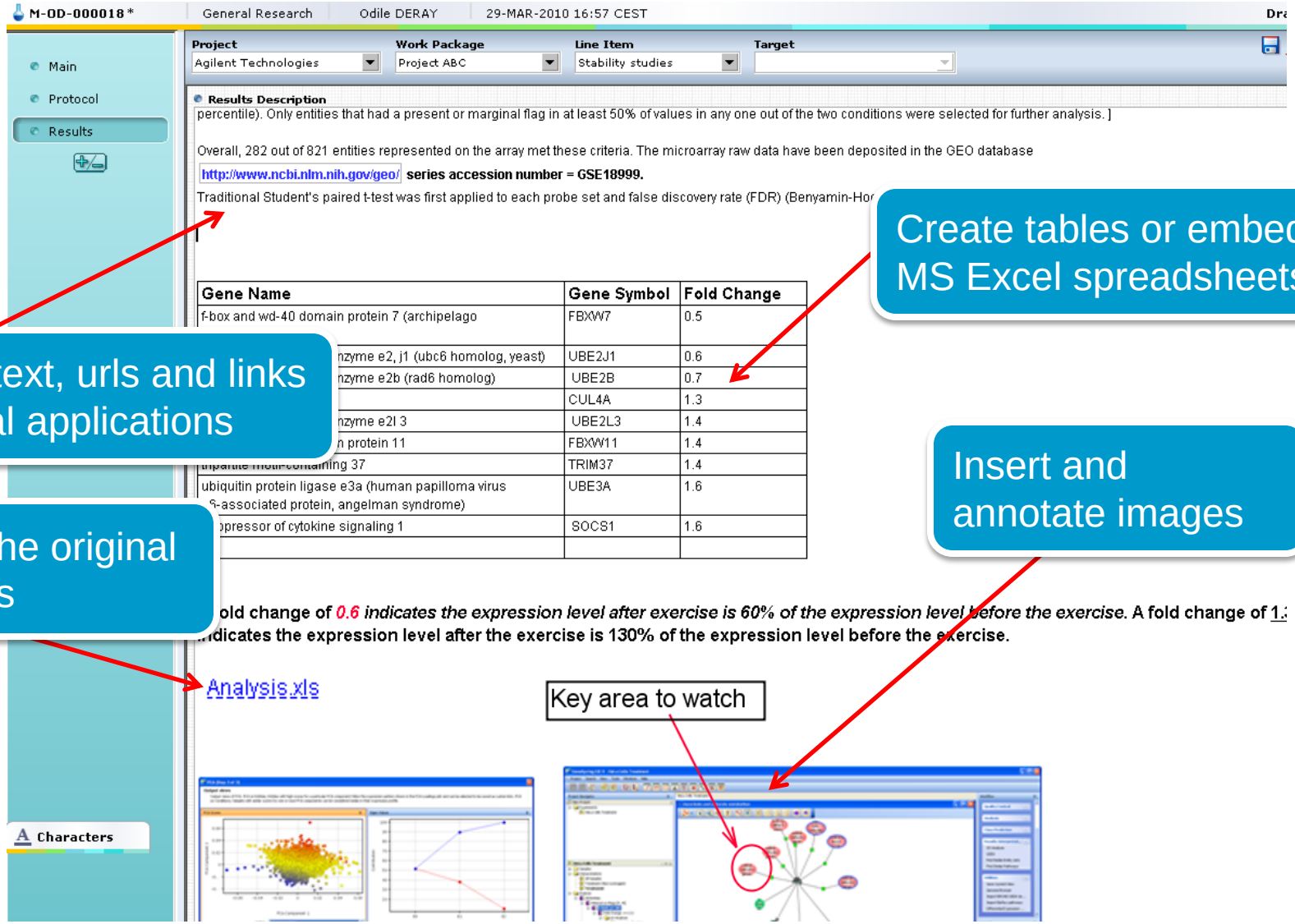
Resulting in…

- Improved efficiency and data quality
- More secure Intellectual Property protection

OpenLAB ELN: Search and re-use protocols and methods

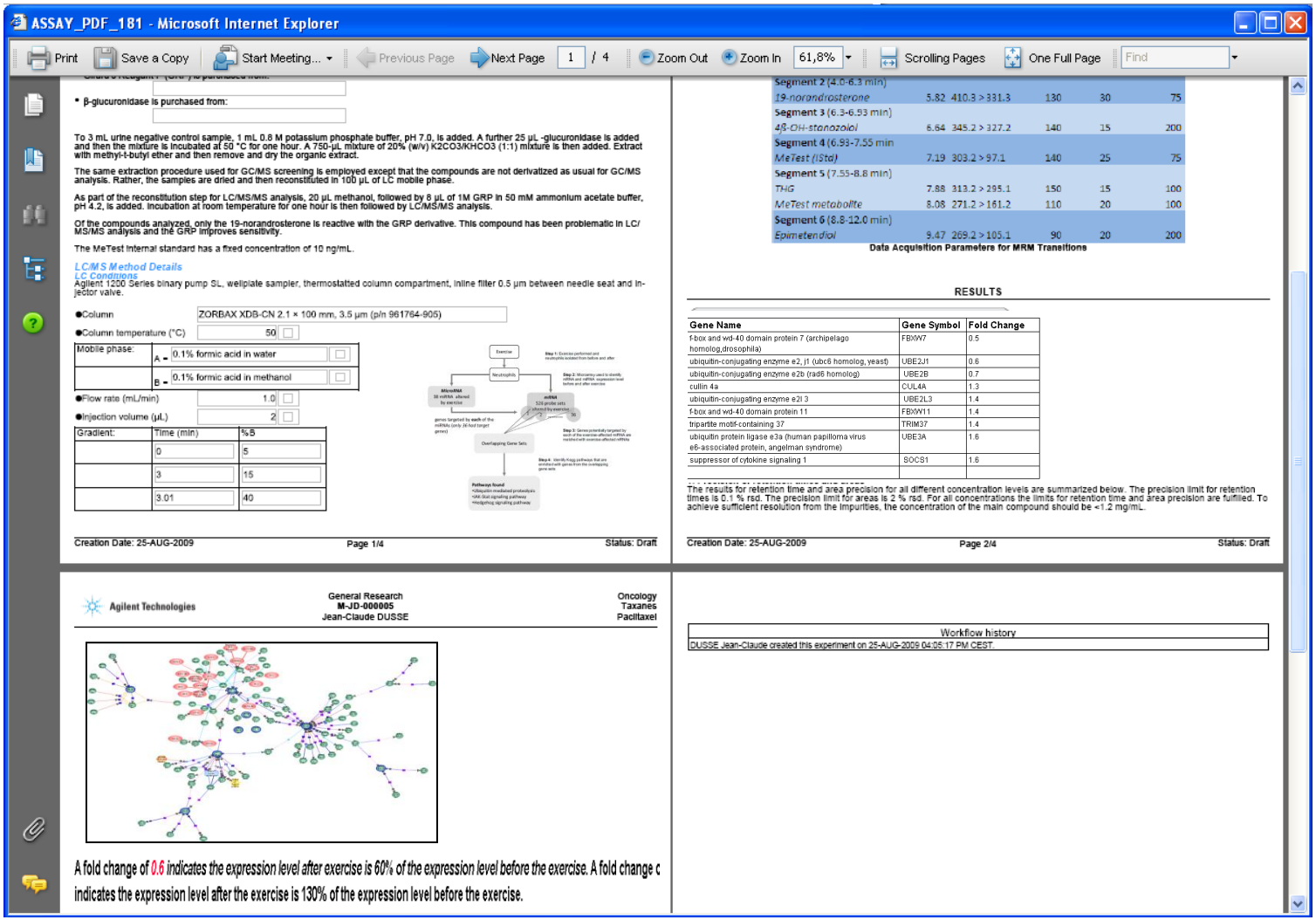


OpenLAB ELN: Experiment results in context

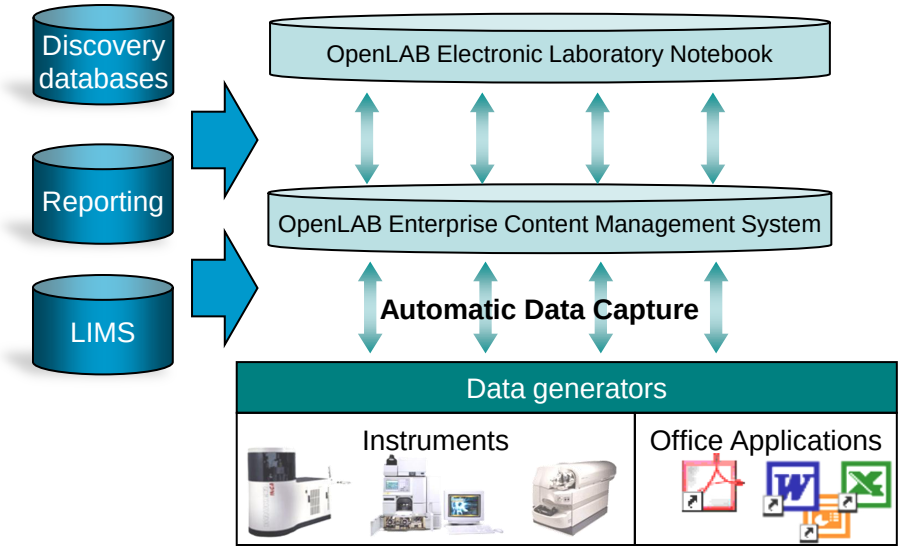


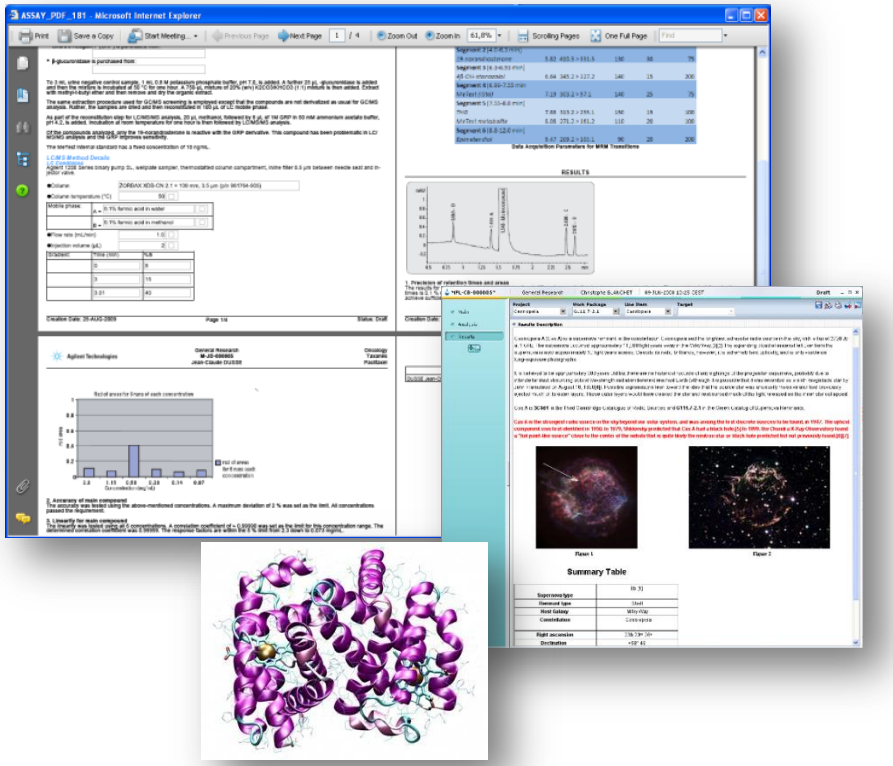
Experiment report contains all data and results

Data traceability and IP protection



Providing a Collaboration Platform





- Enable knowledge management
- Improve IP protection
- Improve regulatory compliance
- Increase productivity

Questions?

Demonstrations available at lunch or after the sessions

Debra.toburen@agilent.com