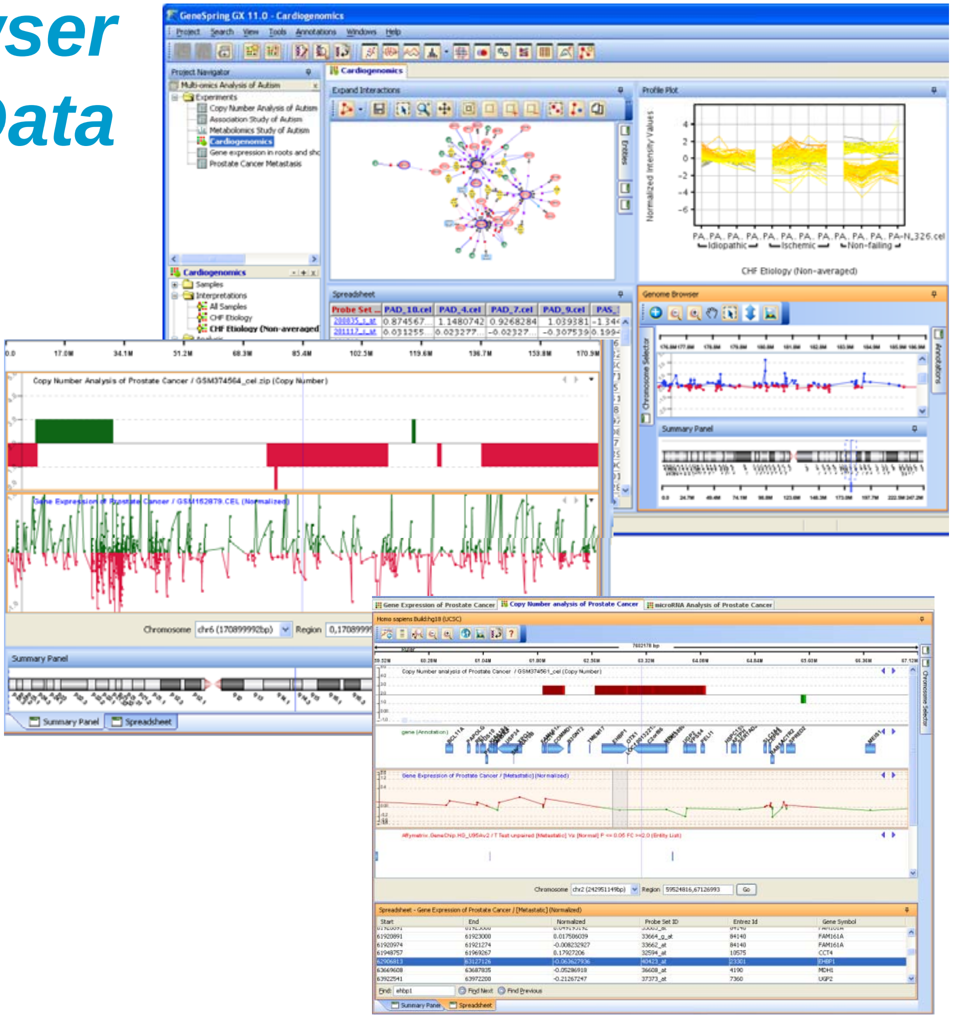
Using the Genome Browser to Explore Genomics Data



Jean Jasinski, Ph.D.
Senior Application Scientist
Mar. 16, 2010

Agilent Technologies

Agenda

Features of Genome Browser

Navigation in Genome Browser

Import and Export of Information from Genome Browser

Methylation and Gene Expression Profiling of Prostate Cancer

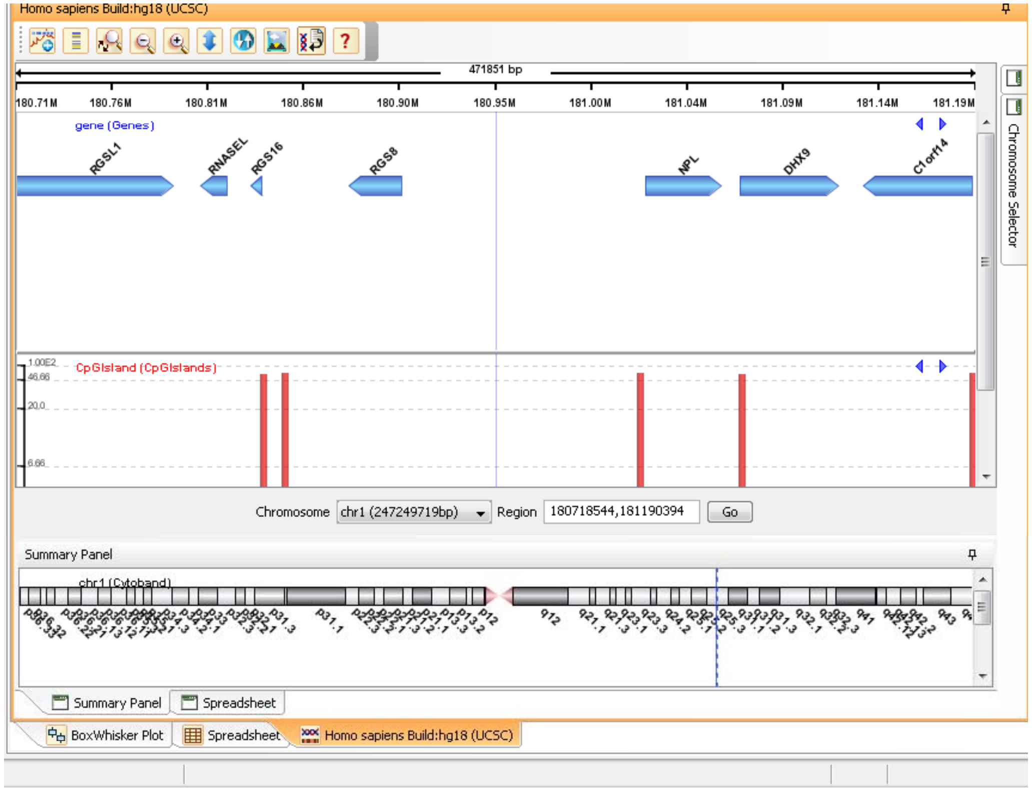
Methylation profiling of prostate cancer (GSE 15298)

- 20 prostate cancer tissues (Cy5); Pooled reference lymphocyte of age matched, healthy men (Cy3)
- Agilent Human 244K CpG Island Array (treated like expression array)

Gene expression profiling of prostate cancer (GSE 3325)

- 6 benign, 6 metastatic prostate cancer, 7 primary prostate cancer
- Affymetrix Human Genome U133 Plus 2.0 Array

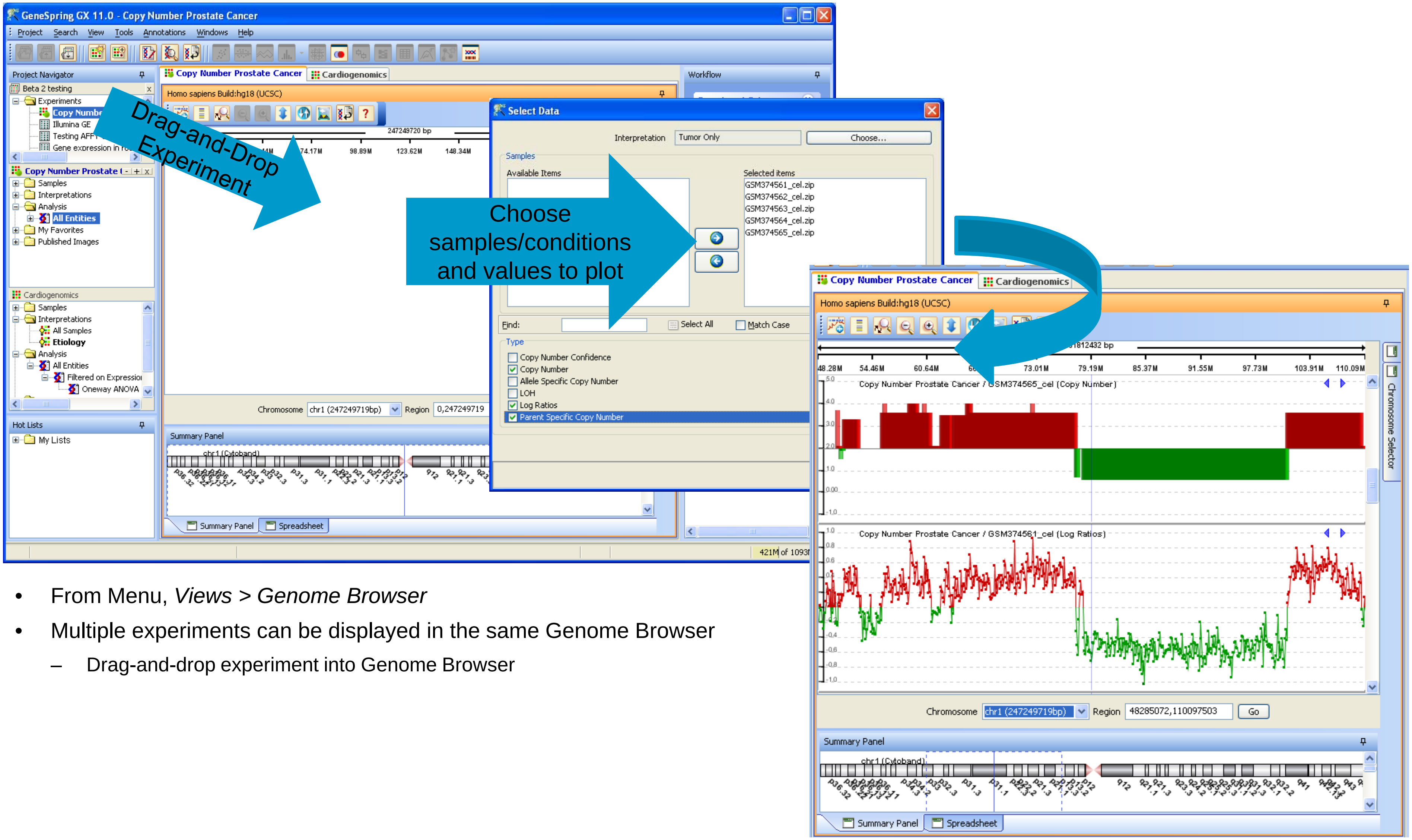
Features of Genome Browser



Chromosome chr1 (247249719bp)

Region 180718544,181190394

Flexible and Interactive Genome Browser



Drag-and-Drop Experiment

Choose samples/conditions and values to plot

Select Data

Interpretation: Tumor Only

Selected items:
GSM374561_cel.zip
GSM374562_cel.zip
GSM374563_cel.zip
GSM374564_cel.zip
GSM374565_cel.zip

Type:
- ☐ Copy Number Confidence
- ☑ Copy Number
- ☐ Allele Specific Copy Number
- ☐ LOH
- ☑ Log Ratios
- ☑ Parent Specific Copy Number

Chromosome: chr1 (247249719bp) Region: 48285072,110097503

- From Menu, *Views* > *Genome Browser*
- Multiple experiments can be displayed in the same Genome Browser
  - Drag-and-drop experiment into Genome Browser

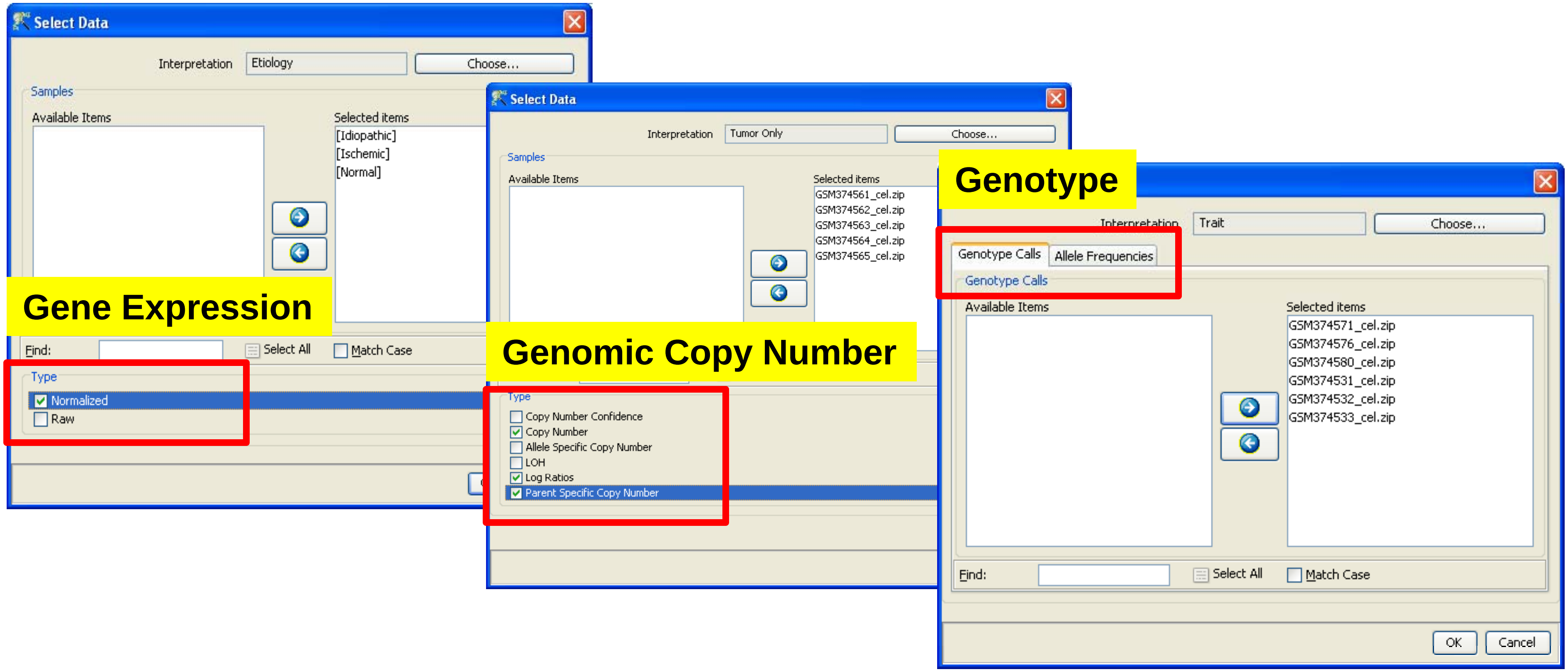
Genome Browser

Three types of objects can be plotted and viewed in Genome Browser

- •Experiment Data
  - – Data can be viewed for individual samples or for conditions
- •Entity List
  - – Plot entities in list by any list-associated values (e.g., fold change, p-values, etc.)*
- •Annotation Track
  - – Import and view annotation tracks in Genome Browser

*Intensity value is not a list-associated value

Plot Experiment Data in Genome Browser



Gene Expression

Interpretation: Etiology

Selected items:
[Idiopathic]
[Ischemic]
[Normal]

Type
☑ Normalized
☐ Raw

Genomic Copy Number

Interpretation: Tumor Only

Selected items:
GSM374561_cel.zip
GSM374562_cel.zip
GSM374563_cel.zip
GSM374564_cel.zip
GSM374565_cel.zip

Type
☐ Copy Number Confidence
☑ Copy Number
☐ Allele Specific Copy Number
☐ LOH
☑ Log Ratios
☑ Parent Specific Copy Number

Genotype

Interpretation: Trait

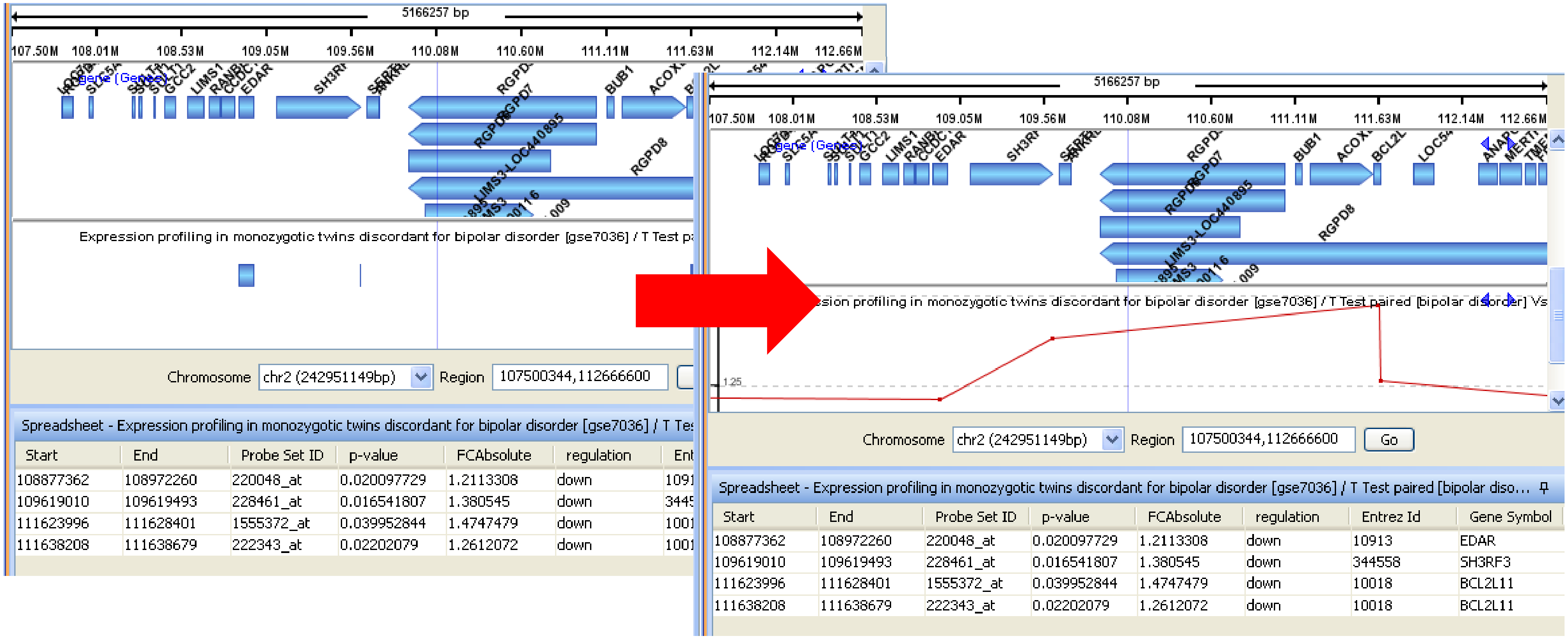
Genotype Calls | Allele Frequencies

Genotype Calls

Selected items:
GSM374571_cel.zip
GSM374576_cel.zip
GSM374580_cel.zip
GSM374531_cel.zip
GSM374532_cel.zip
GSM374533_cel.zip

Options of values to plot depends on experiment type

Plot Entity Lists in Genome Browser



Expression profiling in monozygotic twins discordant for bipolar disorder [gse7036] / T Test paired [bipolar disorder] Vs

Chromosome chr2 (242951149bp) Region 107500344,112666600 Go

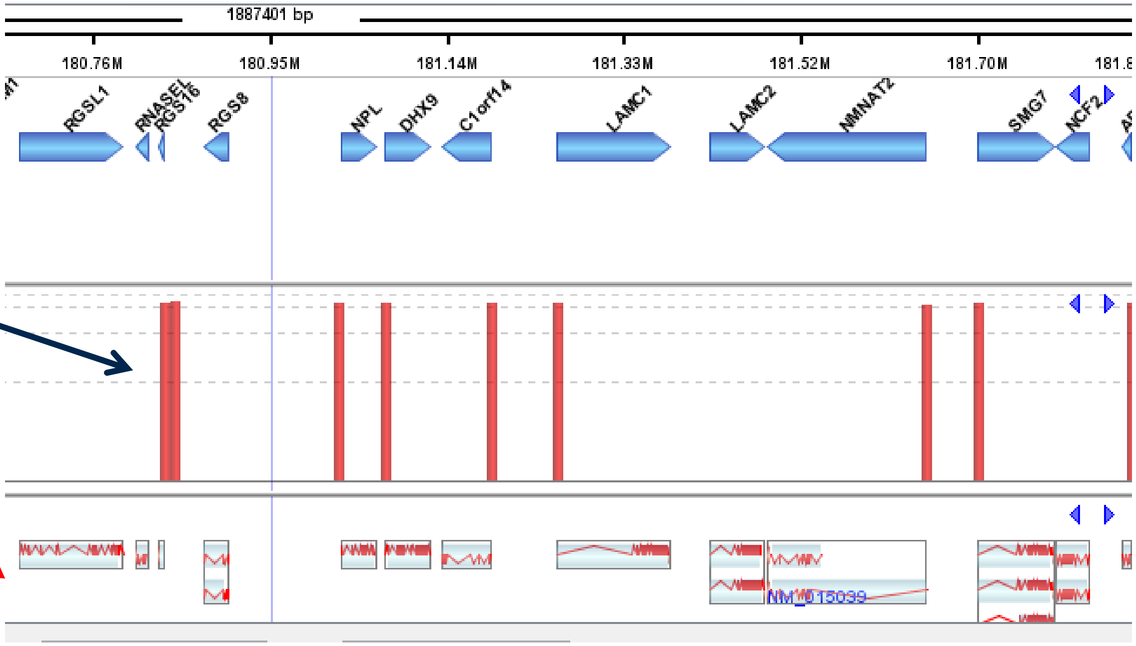
Spreadsheet - Expression profiling in monozygotic twins discordant for bipolar disorder [gse7036] / T Test paired [bipolar diso...

Start	End	Probe Set ID	p-value	FCAbsolute	regulation	Entrez Id	Gene Symbol
108877362	108972260	220048_at	0.020097729	1.2113308	down	10913	EDAR
109619010	109619493	228461_at	0.016541807	1.380545	down	344558	SH3RF3
111623996	111628401	1555372_at	0.039952844	1.4747479	down	10018	BCL2L11
111638208	111638679	222343_at	0.02202079	1.2612072	down	10018	BCL2L11

- By default, Entities in list are plotted as regions by their genomic coordinates
- To plot Entities by their list-associated values (if present): *Right-click > Edit track properties > Rendering > Plot > Select Histogram, Profile, or Scatter > Data column > Select desired column to plot*

Plot Annotation Data in Genome Browser

- Annotations available on the Agilent Server include:



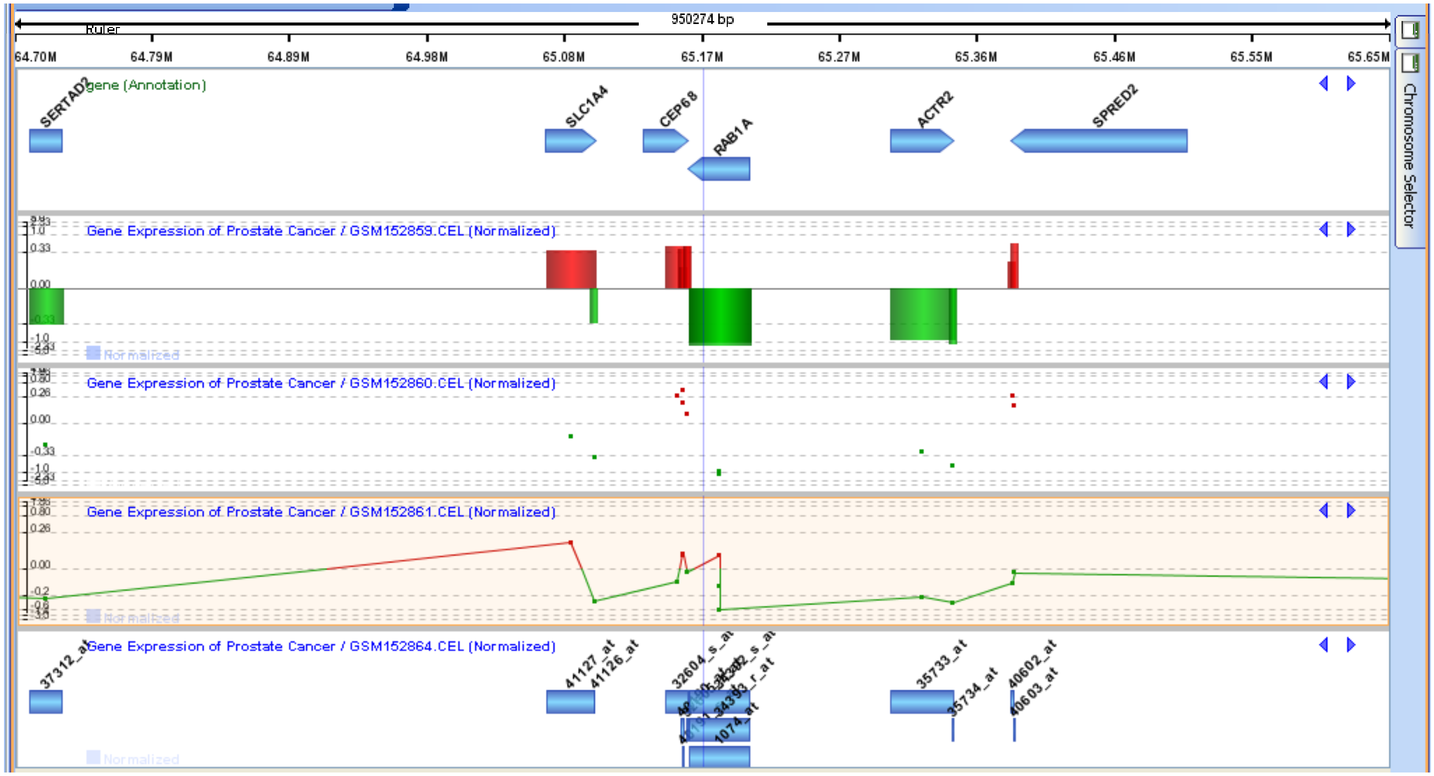
-Gene Track

-CpG Island Track

-Transcript Track

You may also add any kind of annotation tracks that you download from an external source such as UC Santa Cruz or with any annotation file you create.

Track Plot Options in Genome Browser



Annotation Track

Histogram

Scatter Plot

Profile Plot

Region Plot

To choose data plot type: *Right-click on track > Edit Track Properties > Rendering > Plot*

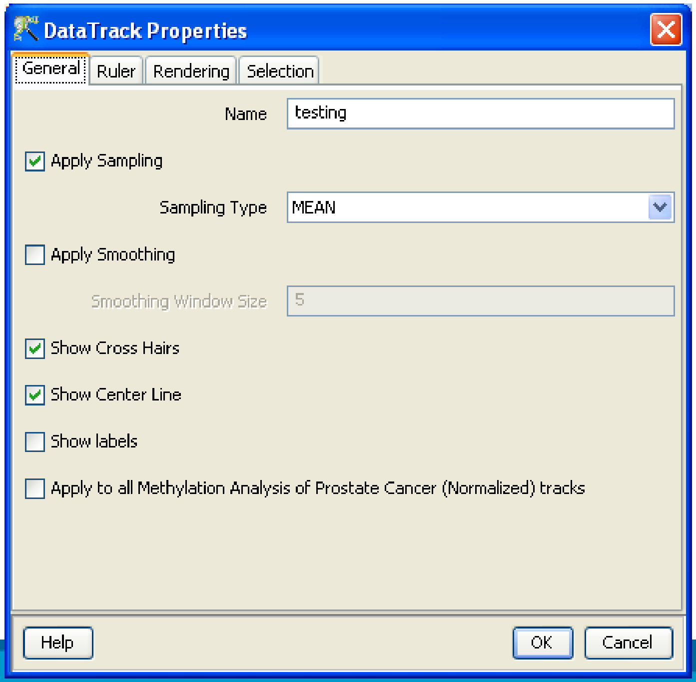
Track Options for Genome Browser

Right-click on track > Change track size

- Change size of selected track, all tracks, or all tracks from the same experiment
- Fit all tracks in view

Right-click on track > Edit track properties

- Rename track
- Change sampling method
- Apply smoothing
- Show label for Entities in track
- Change range of y-axis
- Change plot type
- And more…



Name: testing

☑ Apply Sampling

Sampling Type: MEAN

☐ Apply Smoothing

Smoothing Window Size: 5

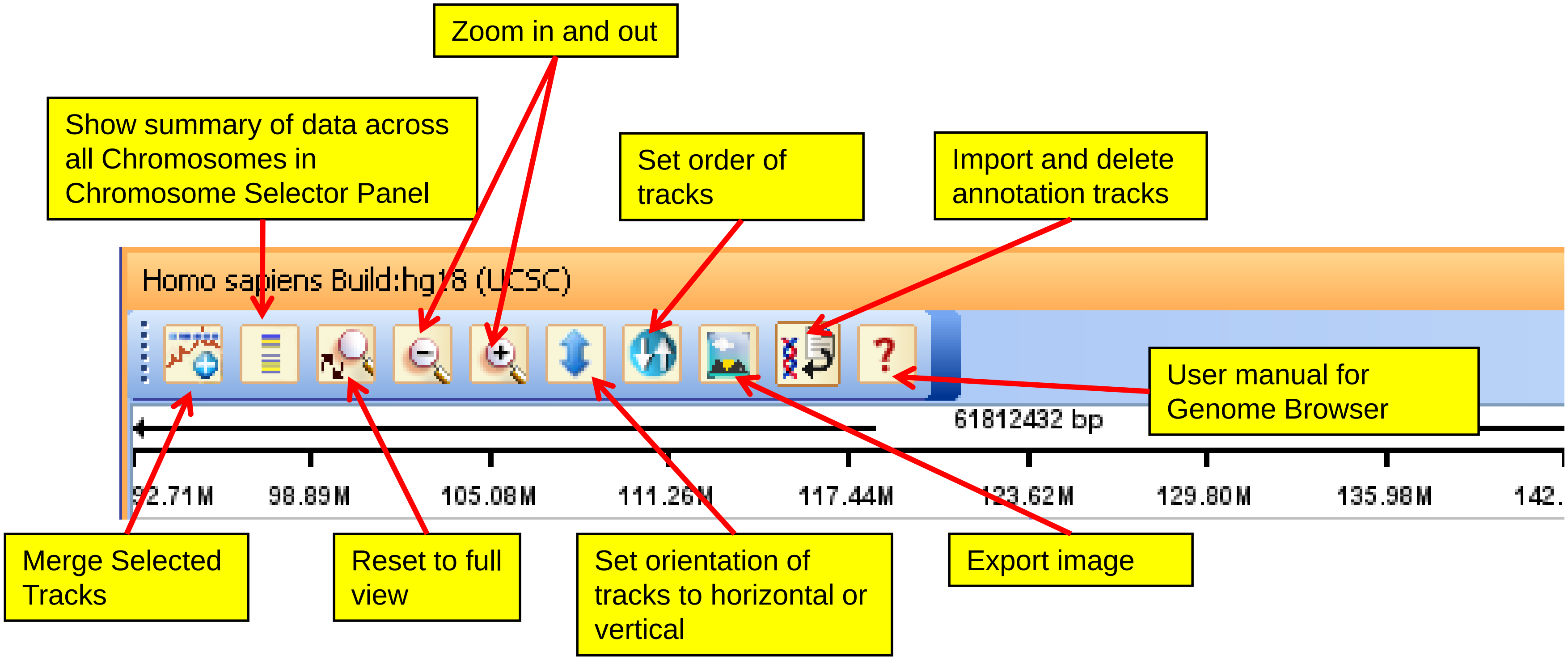
☑ Show Cross Hairs

☑ Show Center Line

☐ Show labels

☐ Apply to all Methylation Analysis of Prostate Cancer (Normalized) tracks

Genome Browser Tool Bar



Zoom in and out

Show summary of data across all Chromosomes in Chromosome Selector Panel

Set order of tracks

Import and delete annotation tracks

User manual for Genome Browser

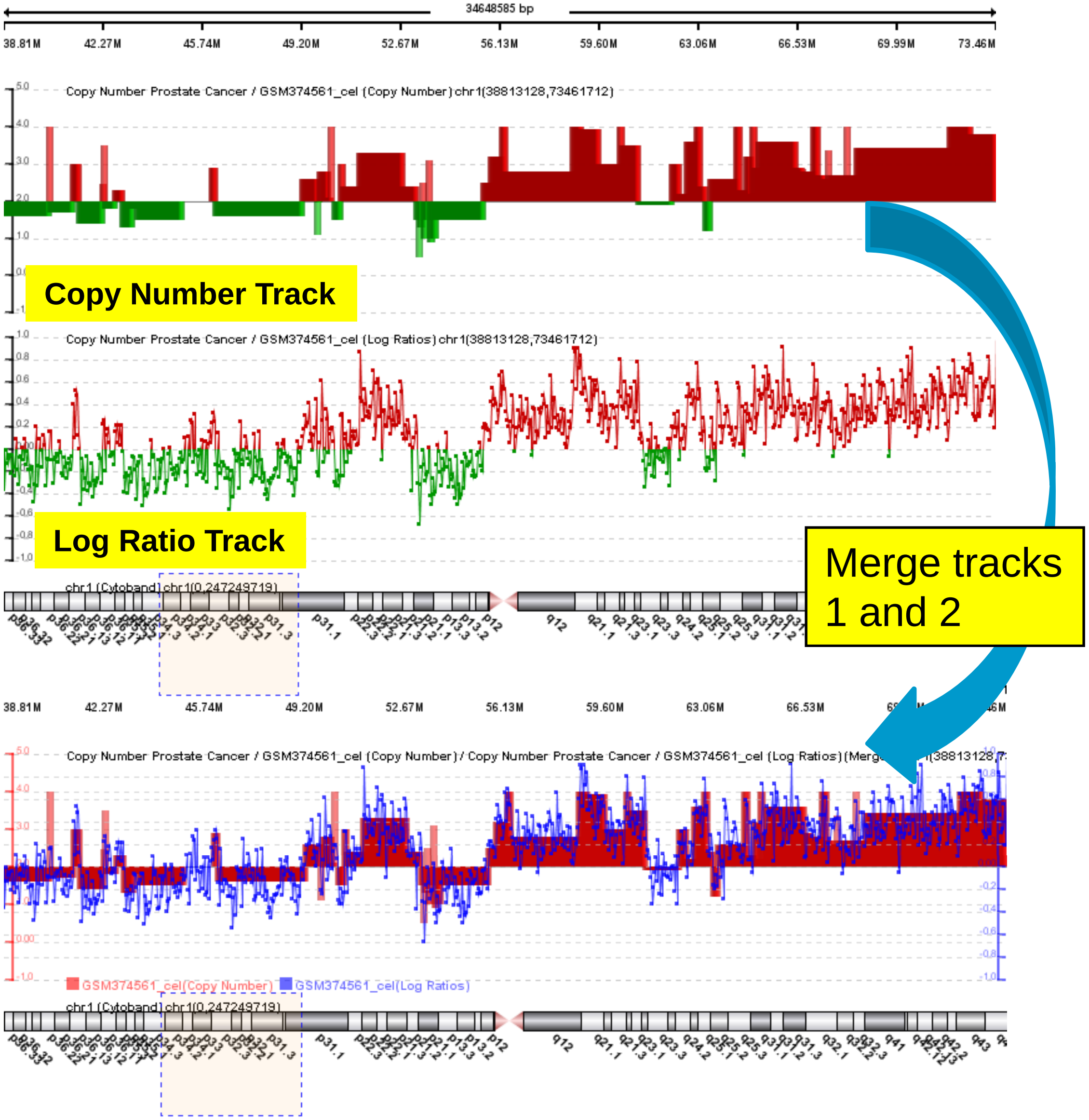
Merge Selected Tracks

Reset to full view

Set orientation of tracks to horizontal or vertical

Export image

Merge Tracks in Genome Browser



Copy Number Track

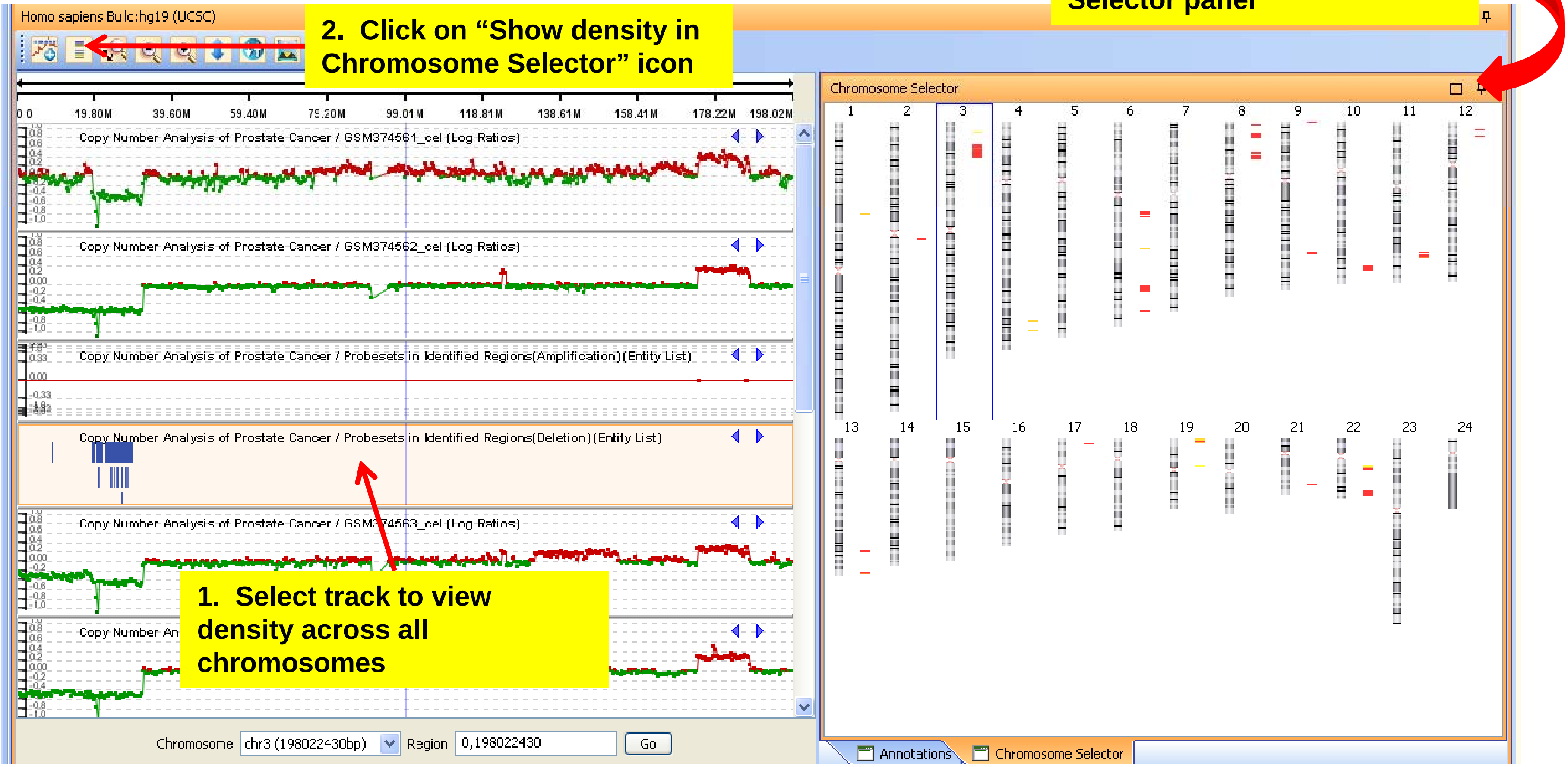
Log Ratio Track

Merge tracks 1 and 2

Data tracks and annotation tracks from same or different Experiments can be merged

- Select multiple tracks using Ctrl + Select
- Click on Merge icon from Genome Browser Toolbar
- To split merged tracks, Right-click > Split tracks

Density View in Genome Browser



Chromosome chr3 (198022430bp) Region 0,198022430

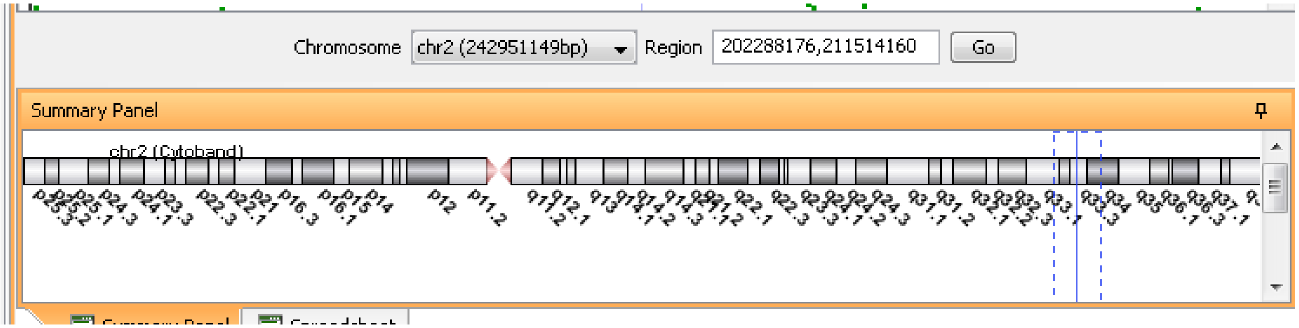
3. Entities in selected track is displayed in Chromosome Selector panel

2. Click on “Show density in Chromosome Selector” icon

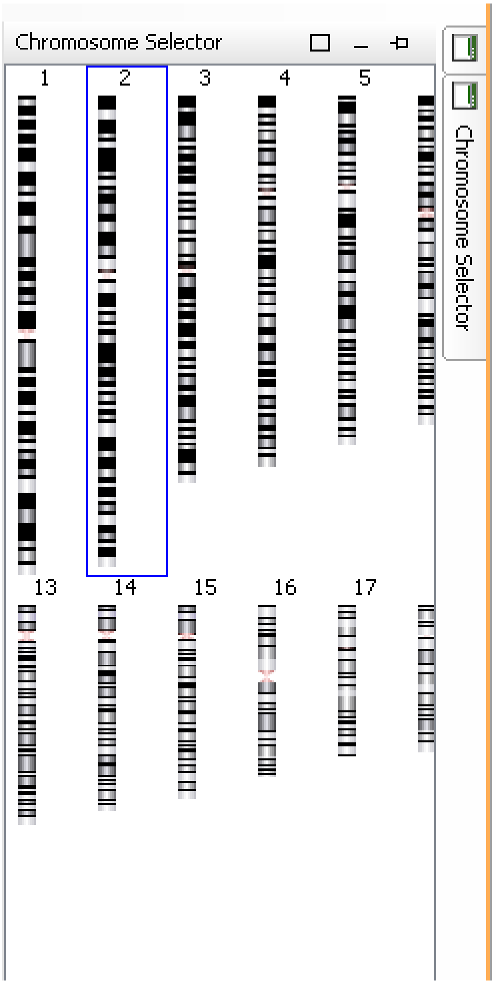
1. Select track to view density across all chromosomes

- Allows you to view all entities in selected track for all chromosomes
- Example: Entity List obtained from Common Genomic Variant Regions Analysis shows regions of common variation in Chromosome Selector panel

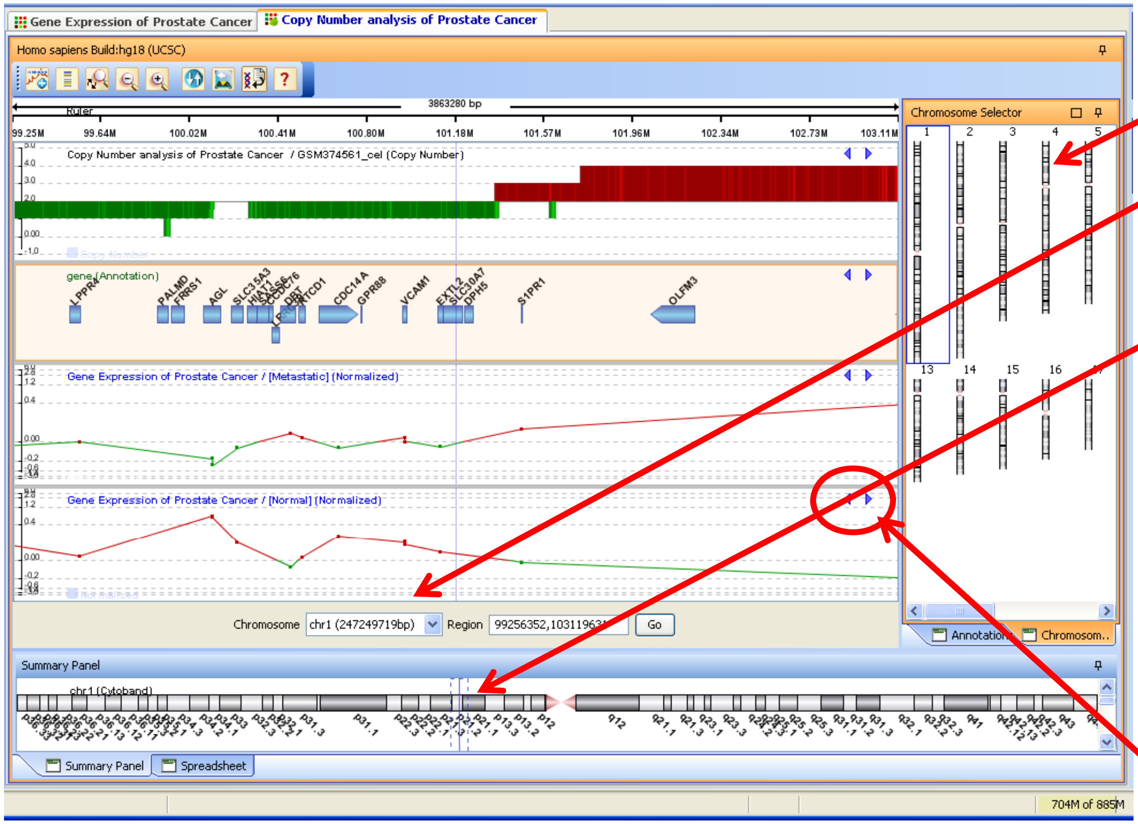
Navigating within Genome Browser



Chromosome chr2 (242951149bp) Region 202288176,211514160



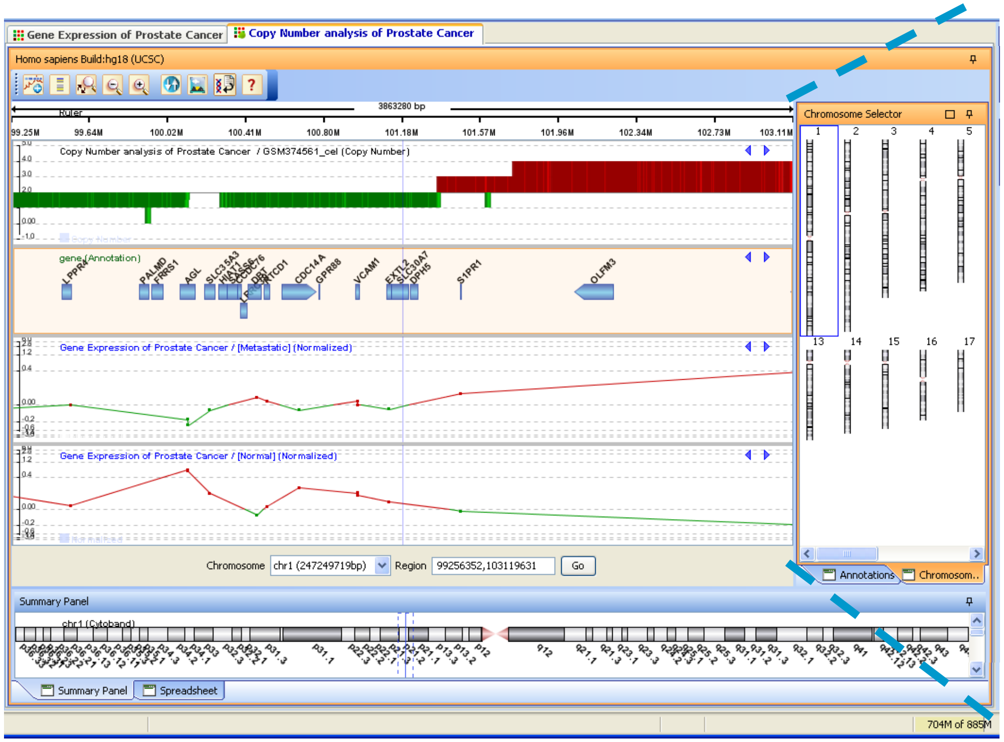
GeneSpring GX 11 Genome Browser Navigation

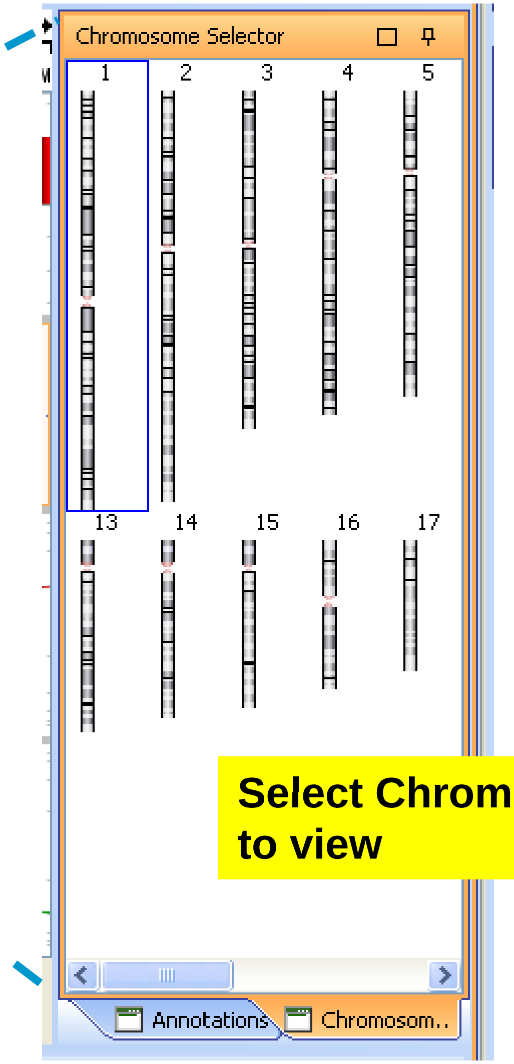


Chromosome chr1 (247249719bp) Region 99256352,10311963 Go

- Jump to Chr of interest:
  - Chr Selector Pane
  - Drop-down menu in window
- Zoom into region of interest:
  - Click drag box in Cytoband view in Summary Panel
  - Shift drag box in any data or annotation track
- Pan around region of interest:
  - Click on any track and drag right-left with mouse
  - Scroll up-down on mouse wheel
  - Use right-left arrows within any track

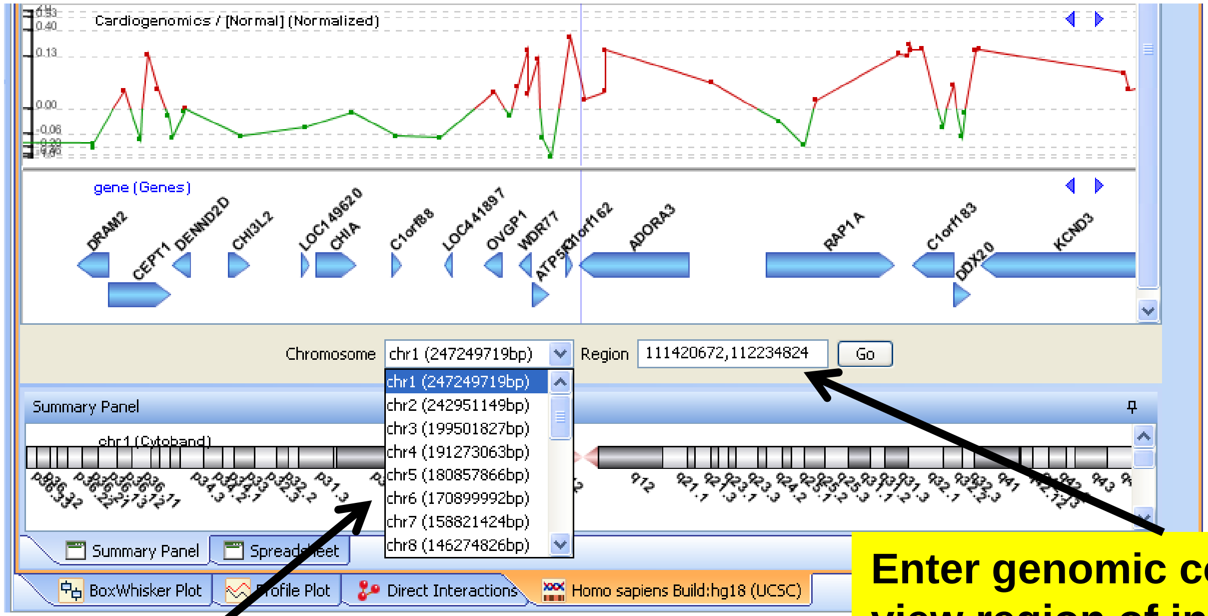
Navigation: Chromosome Selector





Select Chromosome to view

Navigation: Chr Drop-down and Region



Chromosome: chr1 (247249719bp)

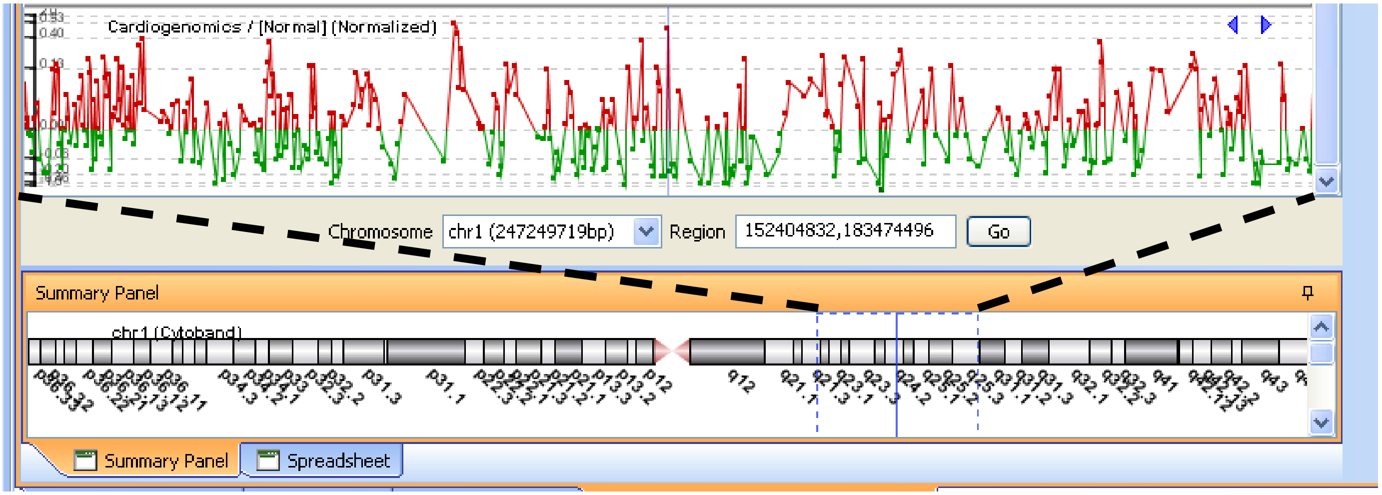
Region: 111420672,112234824

Go

Enter genomic coordinate to view region of interest

Use drop-down menu to select Chromosome to view

Navigation: Cytoband View and Tracks



Cardiogenomics / [Normal] (Normalized)

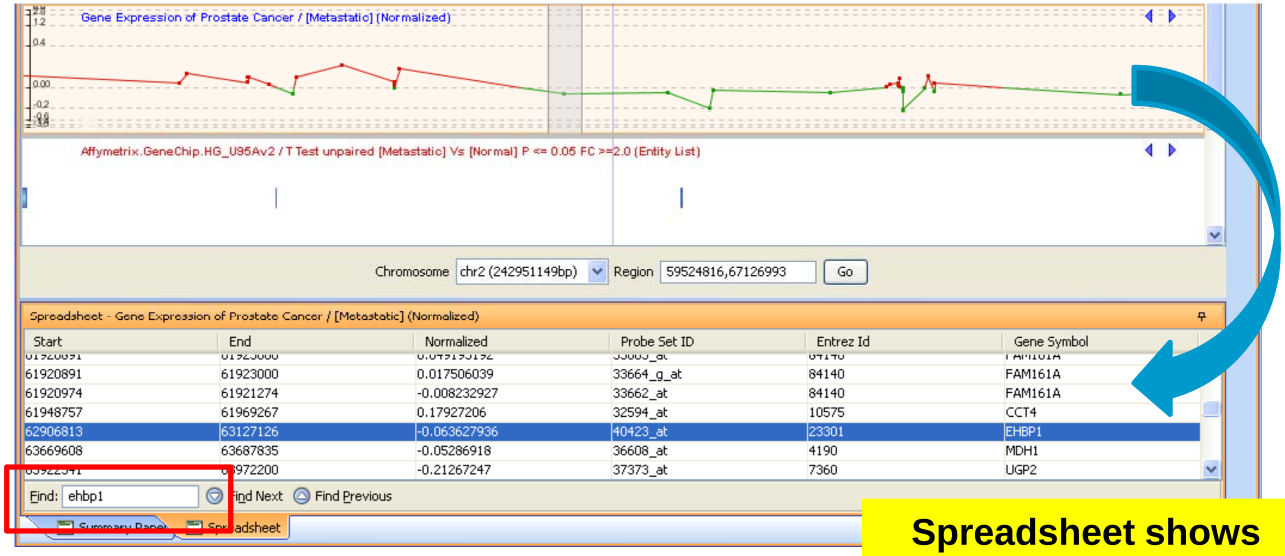
Chromosome chr1 (247249719bp)

Region 152404832,183474496

Navigate to region of interest:

- Click + drag box in Cytoband view in Summary Panel
- Shift + drag box in any data or annotation track

Navigation: Jump to Entity of Interest by Searching in Spreadsheet of Genome Browser



Chromosome: chr2 (242951149bp)

Region: 59524816,67126993

Spreadsheet - Gene Expression of Prostate Cancer / [Metastatic] (Normalized)

Start	End	Normalized	Probe Set ID	Entrez Id	Gene Symbol
61920891	61923000	0.017506039	33664_g_at	84140	FAM161A
61920974	61921274	-0.008232927	33662_at	84140	FAM161A
61948757	61969267	0.17927206	32594_at	10575	CCT4
62906813	63127126	-0.063627936	40423_at	23301	EHBP1
63669608	63687835	-0.05286918	36608_at	4190	MDH1
[illegible]	[illegible]	-0.21267247	37373_at	7360	UGP2

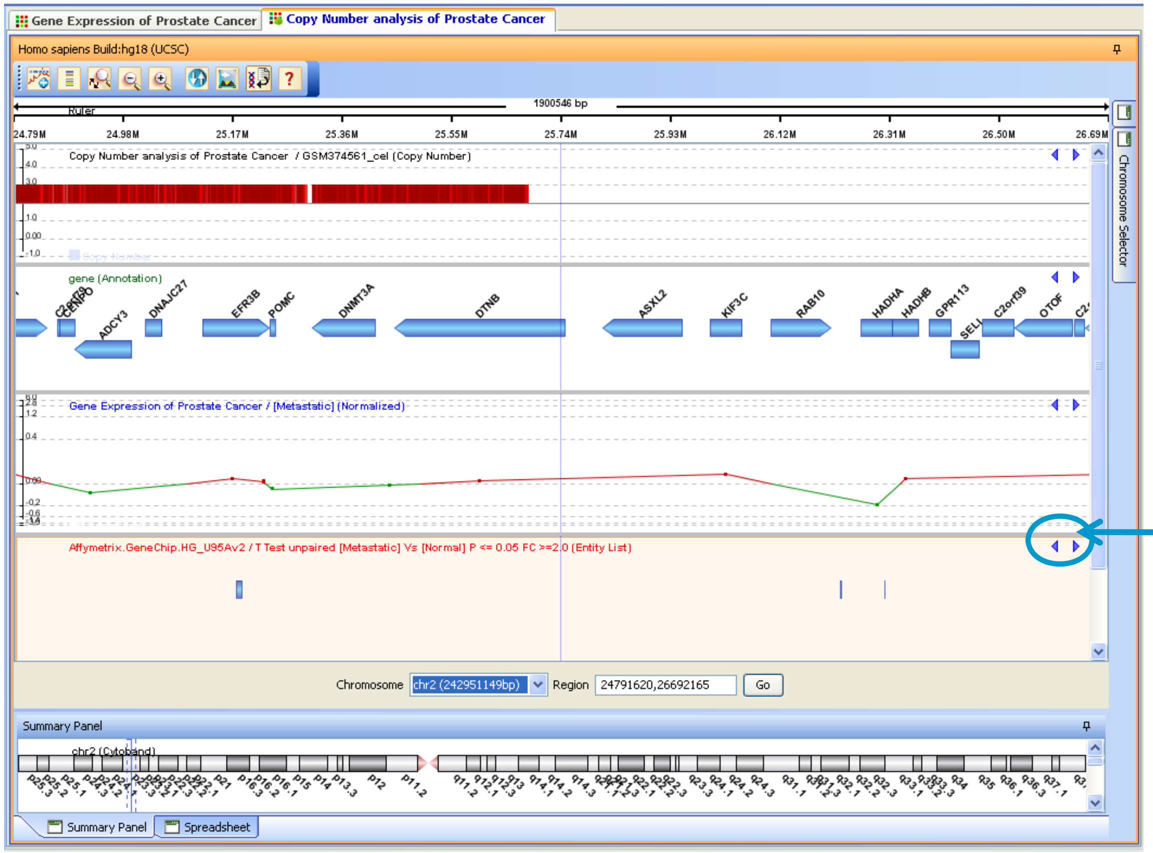
Find: ehbp1

Search for Entity in Spreadsheet

Spreadsheet shows data for selected Track

- Spreadsheet tab displays data for selected track
- Search for Entity of interest using value in any Spreadsheet columns
  - Entity is highlighted in Track and Spreadsheet
  - Double click on Entity in Spreadsheet to zoom into that Entity in Genome Browser

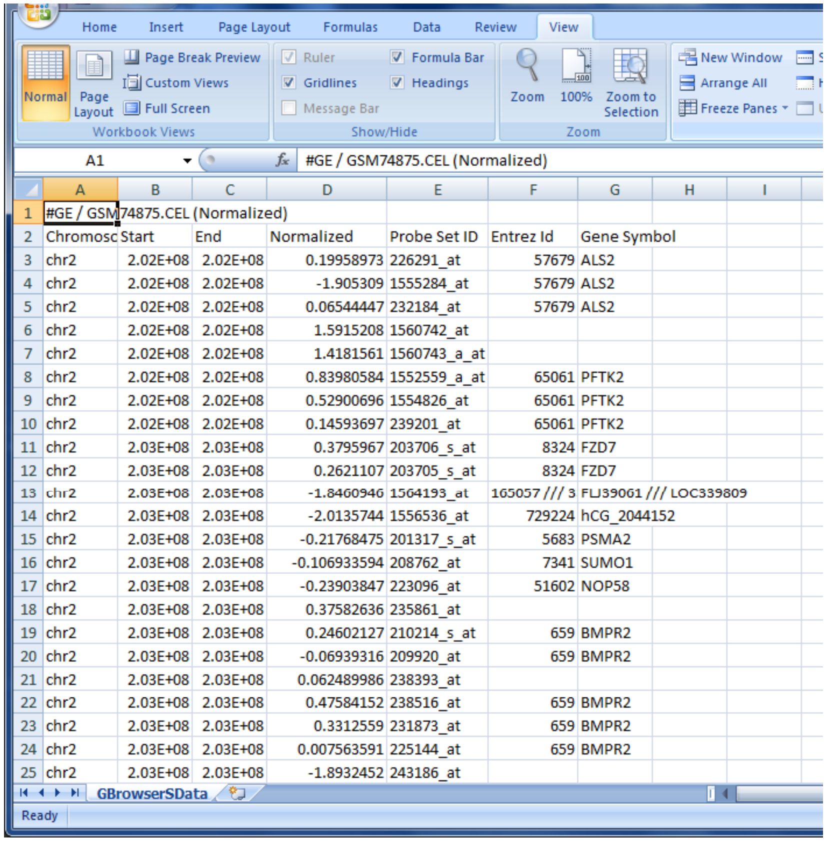
Navigation: Entity List



Chromosome chr2 (242951149bp) Region 24791620,26692165

- Entity Lists can be displayed in Genome Browser and used for navigation of tracks:
  - Drag-n-drop Entity List into Genome Browser
  - Scroll via right-left arrows of Entity List track instructs GeneSpring GX to navigate by jumping to next entity in list

Importing and Exporting Information the Genome Browser



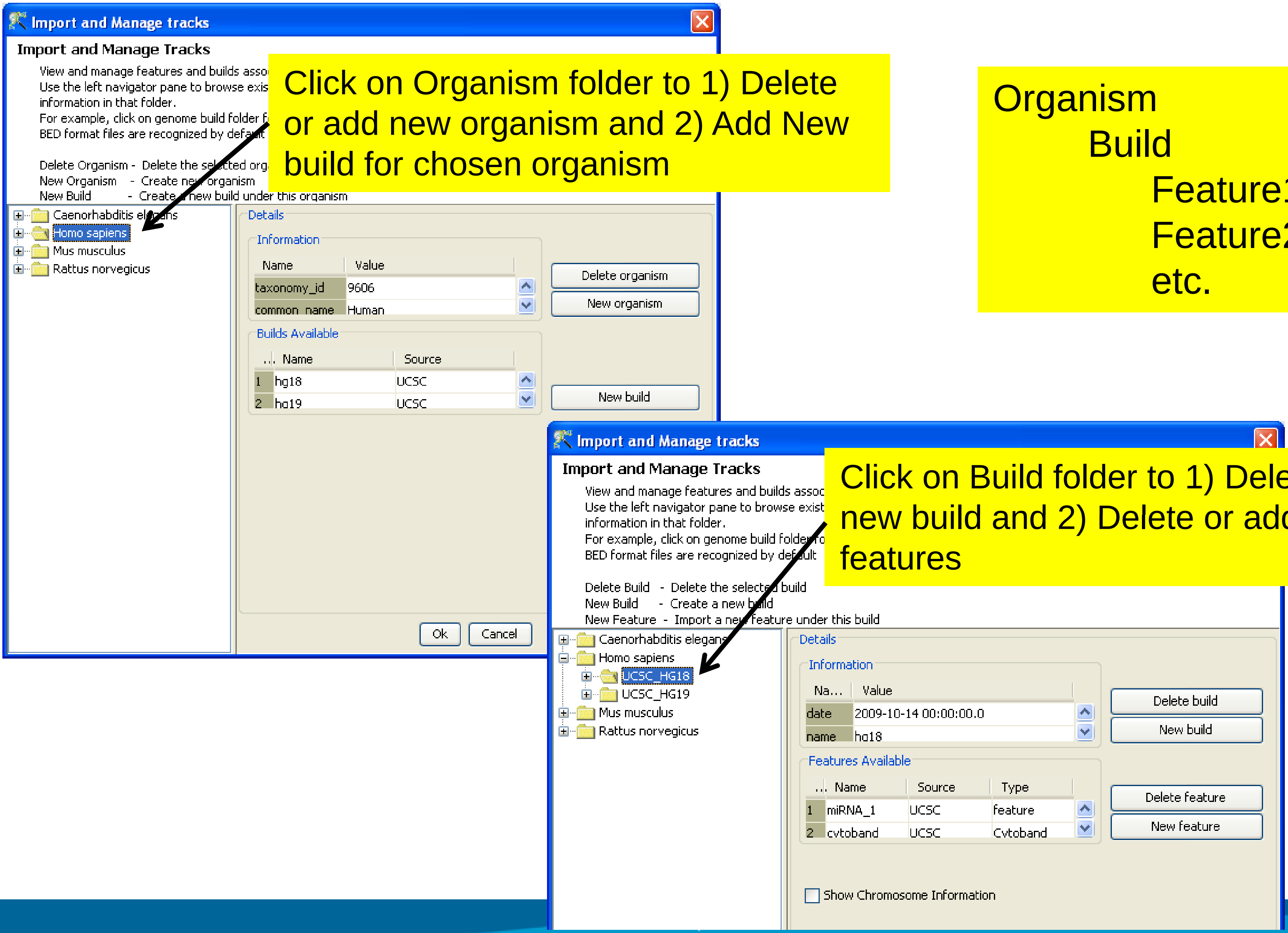
A1: #GE / GSM74875.CEL (Normalized)

	A	B	C	D	E	F	G	H	I
1	#GE / GSM74875.CEL (Normalized)								
2	Chromosc	Start	End	Normalized	Probe Set ID	Entrez Id	Gene Symbol		
3	chr2	2.02E+08	2.02E+08	0.19958973	226291_at	57679	ALS2		
4	chr2	2.02E+08	2.02E+08	-1.905309	1555284_at	57679	ALS2		
5	chr2	2.02E+08	2.02E+08	0.06544447	232184_at	57679	ALS2		
6	chr2	2.02E+08	2.02E+08	1.5915208	1560742_at				
7	chr2	2.02E+08	2.02E+08	1.4181561	1560743_a_at				
8	chr2	2.02E+08	2.02E+08	0.83980584	1552559_a_at	65061	PFTK2		
9	chr2	2.02E+08	2.02E+08	0.52900696	1554826_at	65061	PFTK2		
10	chr2	2.02E+08	2.02E+08	0.14593697	239201_at	65061	PFTK2		
11	chr2	2.03E+08	2.03E+08	0.3795967	203706_s_at	8324	FZD7		
12	chr2	2.03E+08	2.03E+08	0.2621107	203705_s_at	8324	FZD7		
13	chr2	2.03E+08	2.03E+08	-1.8460946	1564193_at	165057 /// 3	FLJ39061 /// LOC339809		
14	chr2	2.03E+08	2.03E+08	-2.0135744	1556536_at	729224	hCG_2044152		
15	chr2	2.03E+08	2.03E+08	-0.21768475	201317_s_at	5683	PSMA2		
16	chr2	2.03E+08	2.03E+08	-0.106933594	208762_at	7341	SUMO1		
17	chr2	2.03E+08	2.03E+08	-0.23903847	223096_at	51602	NOP58		
18	chr2	2.03E+08	2.03E+08	0.37582636	235861_at				
19	chr2	2.03E+08	2.03E+08	0.24602127	210214_s_at	659	BMPR2		
20	chr2	2.03E+08	2.03E+08	-0.06939316	209920_at	659	BMPR2		
21	chr2	2.03E+08	2.03E+08	0.062489986	238393_at				
22	chr2	2.03E+08	2.03E+08	0.47584152	238516_at	659	BMPR2		
23	chr2	2.03E+08	2.03E+08	0.3312559	231873_at	659	BMPR2		
24	chr2	2.03E+08	2.03E+08	0.007563591	225144_at	659	BMPR2		
25	chr2	2.03E+08	2.03E+08	-1.8932452	243186_at				

gene (Genes)(165260992,166301712)

Agilent Technologies

Import and Manage Tracks in Genome Browser



Import and Manage Tracks

View and manage features and builds asso
Use the left navigator pane to browse exis
information in that folder.
For example, click on genome build folder f
BED format files are recognized by default

Delete Organism - Delete the selected org
New Organism - Create new organism
New Build - Create a new build under this organism

Name	Value
taxonomy_id	9606
common_name	Human

...	Name	Source
1	hg18	UCSC
2	hg19	UCSC

Click on Organism folder to 1) Delete or add new organism and 2) Add New build for chosen organism

Organism
Build
Feature1
Feature2
etc.

Import and Manage Tracks

View and manage features and builds assoc
Use the left navigator pane to browse exist
information in that folder.
For example, click on genome build folder fo
BED format files are recognized by default

Delete Build - Delete the selected build
New Build - Create a new build
New Feature - Import a new feature under this build

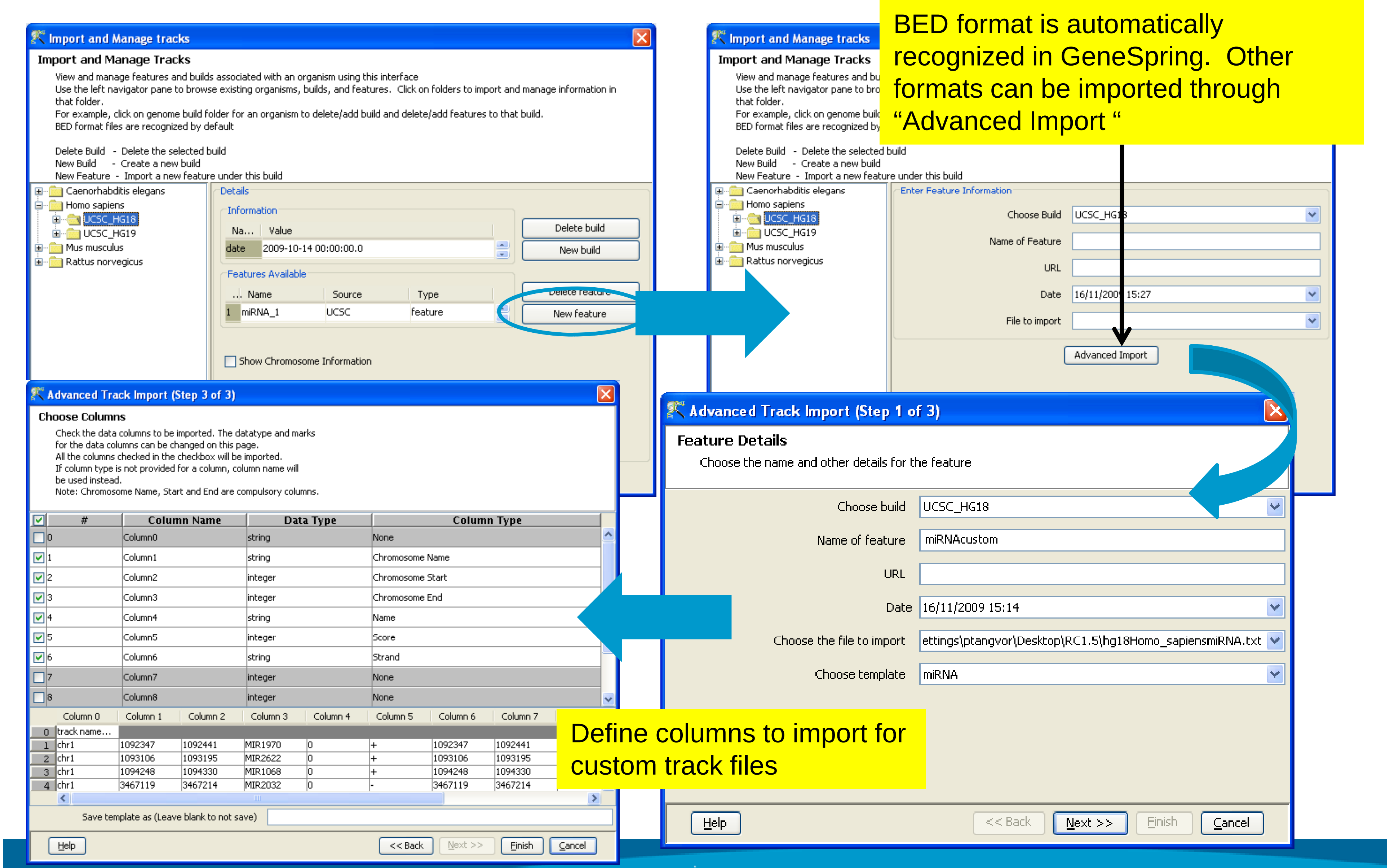
Na...	Value
date	2009-10-14 00:00:00.0
name	hg18

...	Name	Source	Type
1	miRNA_1	UCSC	feature
2	cytoband	UCSC	Cytoband

☐ Show Chromosome Information

Click on Build folder to 1) Delete or add new build and 2) Delete or add track features

Import Tracks for Viewing in Genome Browser



Import and Manage tracks

Import and Manage Tracks

View and manage features and builds associated with an organism using this interface
Use the left navigator pane to browse existing organisms, builds, and features. Click on folders to import and manage information in that folder.
For example, click on genome build folder for an organism to delete/add build and delete/add features to that build.
BED format files are recognized by default

Delete Build - Delete the selected build
New Build - Create a new build
New Feature - Import a new feature under this build

- Caenorhabditis elegans
- Homo sapiens
  - UCSC_HG18
  - UCSC_HG19
- Mus musculus
- Rattus norvegicus

Details

Information

Na...	Value
date	2009-10-14 00:00:00.0

Features Available

...	Name	Source	Type
1	miRNA_1	UCSC	feature

☐ Show Chromosome Information

BED format is automatically recognized in GeneSpring. Other formats can be imported through “Advanced Import “

Import and Manage tracks

Enter Feature Information

Choose Build: UCSC_HG18
Name of Feature:
URL:
Date: 16/11/2009 15:27
File to import:

Advanced Track Import (Step 1 of 3)

Feature Details

Choose the name and other details for the feature

Choose build: UCSC_HG18
Name of feature: miRNAcustom
URL:
Date: 16/11/2009 15:14
Choose the file to import: ettings\ptangvor\Desktop\RC1.5\hg18Homo_sapiensmiRNA.txt
Choose template: miRNA

Advanced Track Import (Step 3 of 3)

Choose Columns

Check the data columns to be imported. The datatype and marks for the data columns can be changed on this page.
All the columns checked in the checkbox will be imported.
If column type is not provided for a column, column name will be used instead.
Note: Chromosome Name, Start and End are compulsory columns.

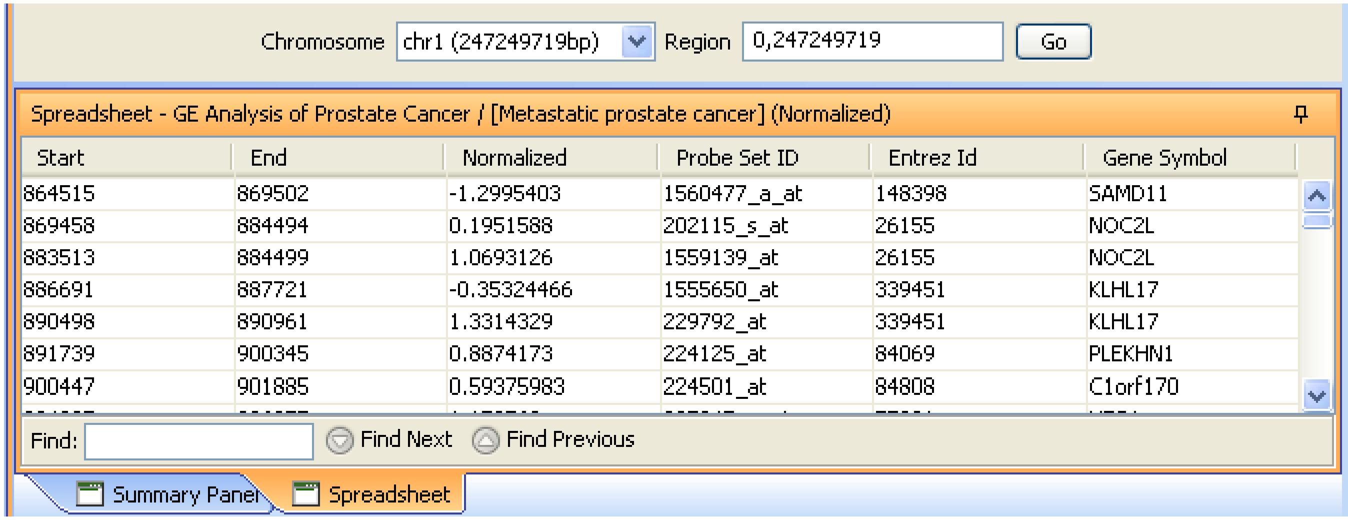
☑	#	Column Name	Data Type	Column Type
☐	0	Column0	string	None
☑	1	Column1	string	Chromosome Name
☑	2	Column2	integer	Chromosome Start
☑	3	Column3	integer	Chromosome End
☑	4	Column4	string	Name
☑	5	Column5	integer	Score
☑	6	Column6	string	Strand
☐	7	Column7	integer	None
☐	8	Column8	integer	None

	Column 0	Column 1	Column 2	Column 3	Column 4	Column 5	Column 6	Column 7
0	track name...							
1	chr1	1092347	1092441	MIR1970	0	+	1092347	1092441
2	chr1	1093106	1093195	MIR2622	0	+	1093106	1093195
3	chr1	1094248	1094330	MIR1068	0	+	1094248	1094330
4	chr1	3467119	3467214	MIR2032	0	-	3467119	3467214

Save template as (Leave blank to not save):

Define columns to import for custom track files

Exporting Information in Spreadsheet



Chromosome chr1 (247249719bp) Region 0,247249719

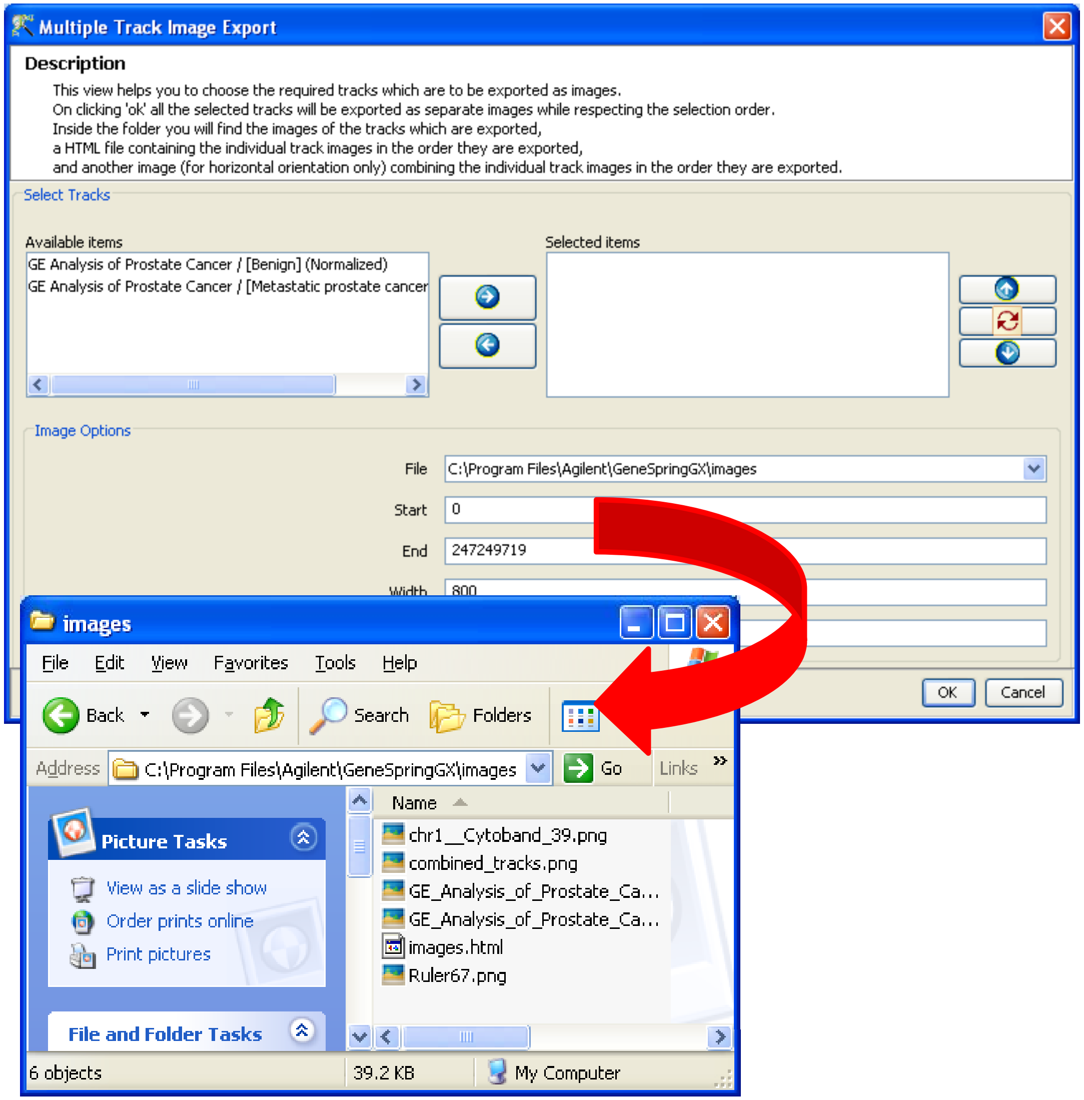
Spreadsheet - GE Analysis of Prostate Cancer / [Metastatic prostate cancer] (Normalized)

Start	End	Normalized	Probe Set ID	Entrez Id	Gene Symbol
864515	869502	-1.2995403	1560477_a_at	148398	SAMD11
869458	884494	0.1951588	202115_s_at	26155	NOC2L
883513	884499	1.0693126	1559139_at	26155	NOC2L
886691	887721	-0.35324466	1555650_at	339451	KLHL17
890498	890961	1.3314329	229792_at	339451	KLHL17
891739	900345	0.8874173	224125_at	84069	PLEKHN1
900447	901885	0.59375983	224501_at	84808	C1orf170

Right-click on Spreadsheet:

- Export as Entity List
  - Creates Entity List in Navigator containing Entities in Spreadsheet
- Export as Text
  - Creates text (.tsv) file containing Spreadsheet information

Export Track Images



Description

This view helps you to choose the required tracks which are to be exported as images.
On clicking 'ok' all the selected tracks will be exported as separate images while respecting the selection order.
Inside the folder you will find the images of the tracks which are exported,
a HTML file containing the individual track images in the order they are exported,
and another image (for horizontal orientation only) combining the individual track images in the order they are exported.

Available items:
- GE Analysis of Prostate Cancer / [Benign] (Normalized)
- GE Analysis of Prostate Cancer / [Metastatic prostate cancer

File: C:\Program Files\Agilent\GeneSpringGX\images
Start: 0
End: 247249719
Width: 800

Address: C:\Program Files\Agilent\GeneSpringGX\images

- chr1__Cytoband_39.png
- combined_tracks.png
- GE_Analysis_of_Prostate_Ca...
- GE_Analysis_of_Prostate_Ca...
- images.html
- Ruler67.png

To export image for a single track: *Right-click on track > Export as > Image*

To export multiple tracks and Genome Browser components: *Click on "Export Select Track as Image" icon from Toolbar*

- Select tracks to export
- Set Image Options for export
- Folder containing exported images:
  - Individual images of selected tracks
  - Cytoband and Ruler of Genome Browser
  - Entire view as displayed in Genome Browser (png and html)

Thank you for your attention

Questions?