

MANTRA 2.0 TUTORIAL



mantra.tigem.it



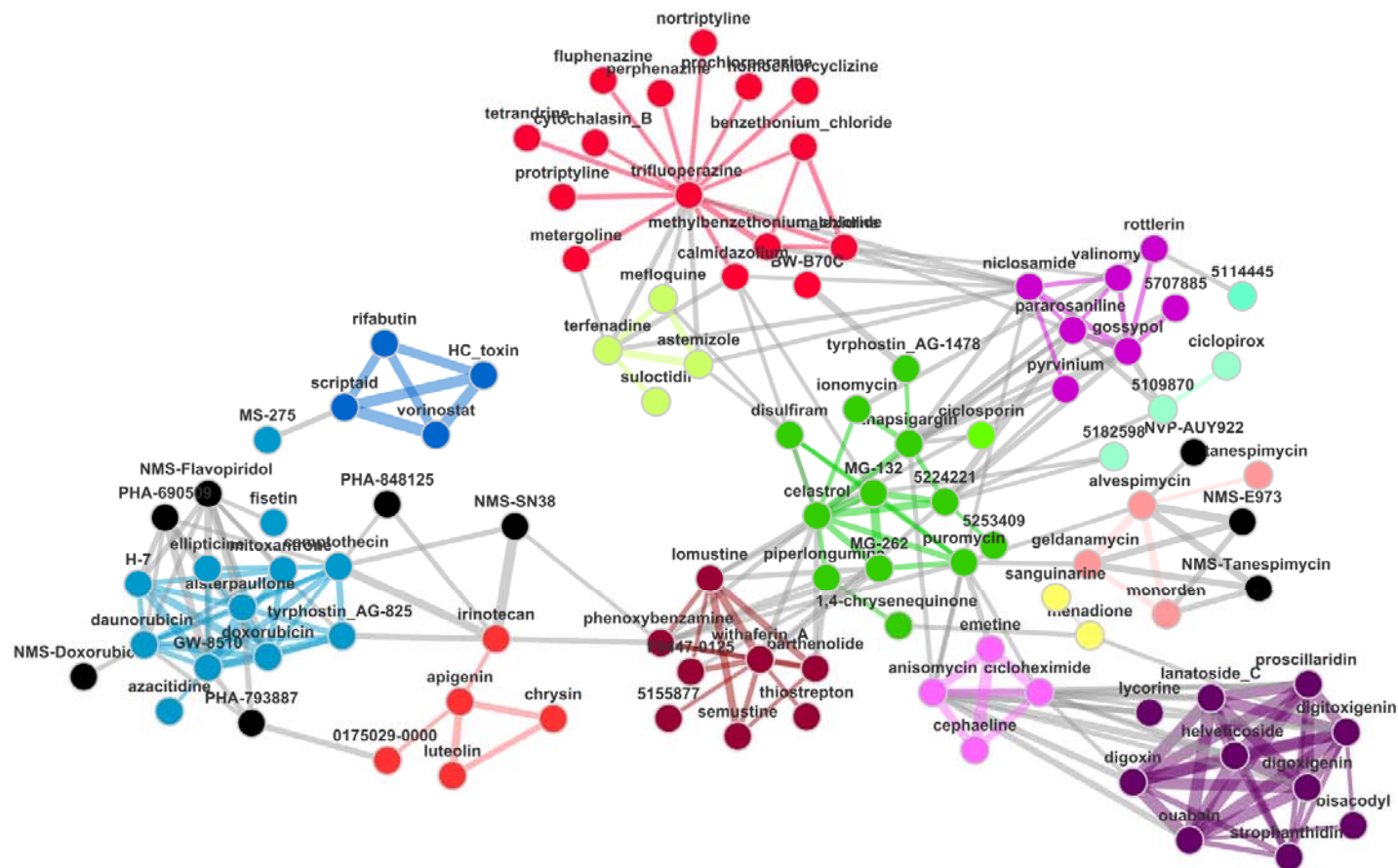
OUTLINE



1. MANTRA Web Tool
2. Analysis
 - a) New Experiment
 - b) New Node
 - c) GSEA
3. Network
 - a) View
 - b) Button Panel
4. Search
5. In Summary
6. Conclusion

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2. Analysis
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MANTRA (Mode of Action by NeTwoRk Analysis) is a software tool for the analysis of the Mode of Action (MoA) of drugs and for “drug repositioning”. It is based on network theory and non-parametric statistics on gene expression data.



1. Database for add and storage of experiments, nodes, and distance matrix
2. Annotation and editing tools for nodes
3. Deleting nodes
4. Integration of a pipeline of microarray analysis
5. Downloading tabulated results and Cytoscape file (.sif format)
6. Common genes analysis
7. Advanced search for nodes
8. Gene set enrichment analysis



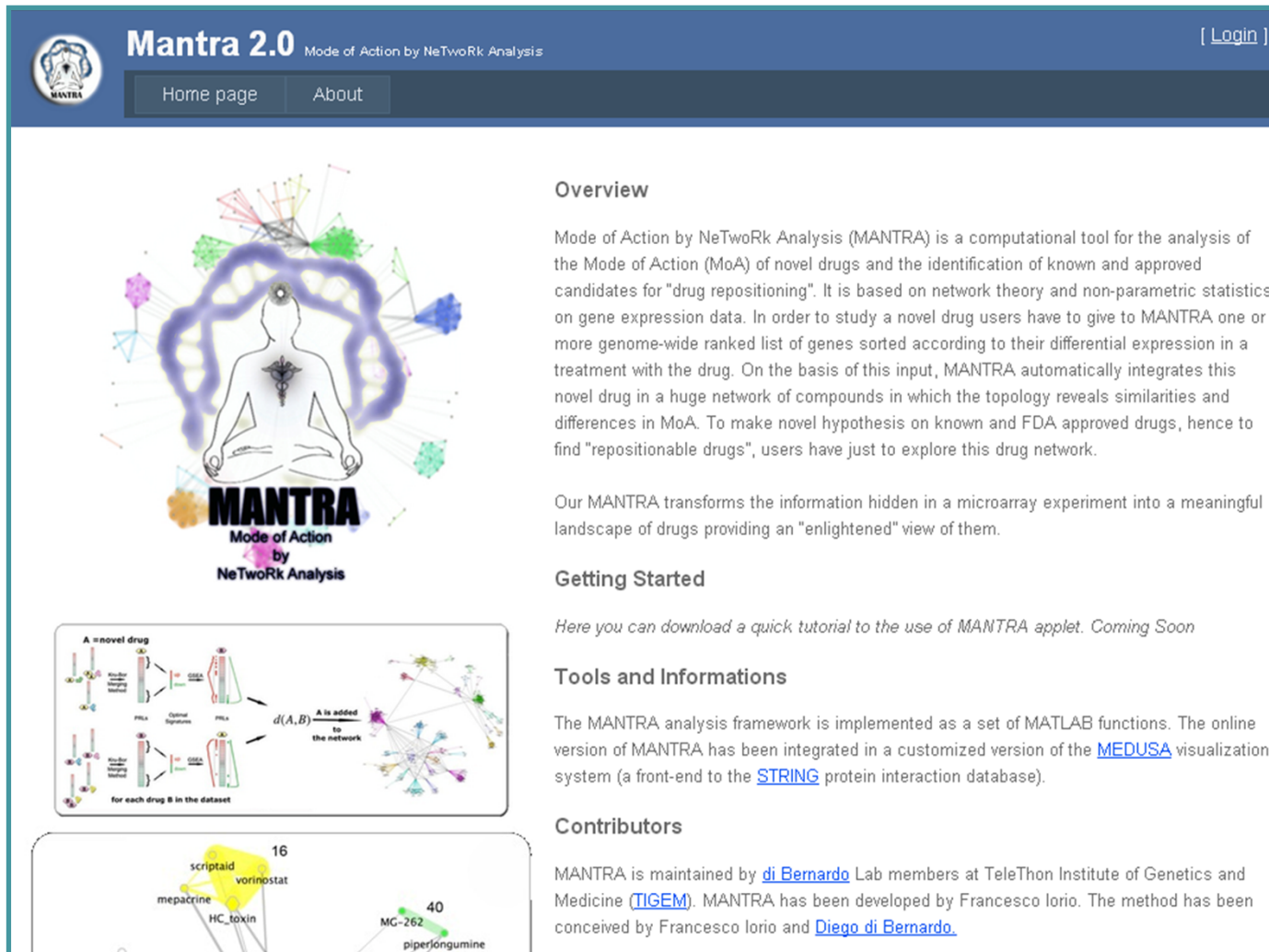


MANTRA WEB TOOL - Mantra 2.0 Features




- MANTRA 2.0 has been implemented by customizing the Applet version of Medusa (Hooper and Bork, 2005), a front end for protein interaction databases, which can be also used as a general graph visualization tool.
- The MANTRA 2.0 implements the method in (Iorio, et al., 2010) for the discovery of drug MoA and the repositioning of known drugs from the analysis of transcriptional responses.
- It allows users to visually explore the Drug Network that we inferred for 1309 compounds in a user-friendly environment providing, for each of the drugs, information about biochemical interactions, therapeutic indications, known MoA, pharmacology and targeted proteins.
- By exploring the Drug Network, users can identify unexpected similarities between drugs acting on different direct intra-cellular targets and search for “repositionable” drugs.

To access the web-tool click on “**Login**” in top right.



Mantra 2.0 Mode of Action by NeTwoRk Analysis [[Login](#)]

[Home page](#) [About](#)



MANTRA
Mode of Action
by
NeTwoRk Analysis

Overview

Mode of Action by NeTwoRk Analysis (MANTRA) is a computational tool for the analysis of the Mode of Action (MoA) of novel drugs and the identification of known and approved candidates for "drug repositioning". It is based on network theory and non-parametric statistics on gene expression data. In order to study a novel drug users have to give to MANTRA one or more genome-wide ranked list of genes sorted according to their differential expression in a treatment with the drug. On the basis of this input, MANTRA automatically integrates this novel drug in a huge network of compounds in which the topology reveals similarities and differences in MoA. To make novel hypothesis on known and FDA approved drugs, hence to find "repositionable drugs", users have just to explore this drug network.

Our MANTRA transforms the information hidden in a microarray experiment into a meaningful landscape of drugs providing an "enlightened" view of them.

Getting Started

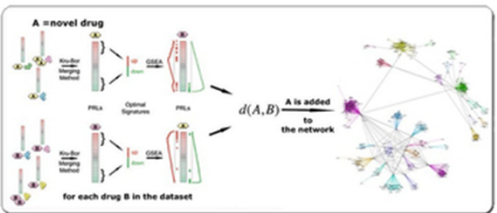

Here you can download a quick tutorial to the use of MANTRA applet. Coming Soon

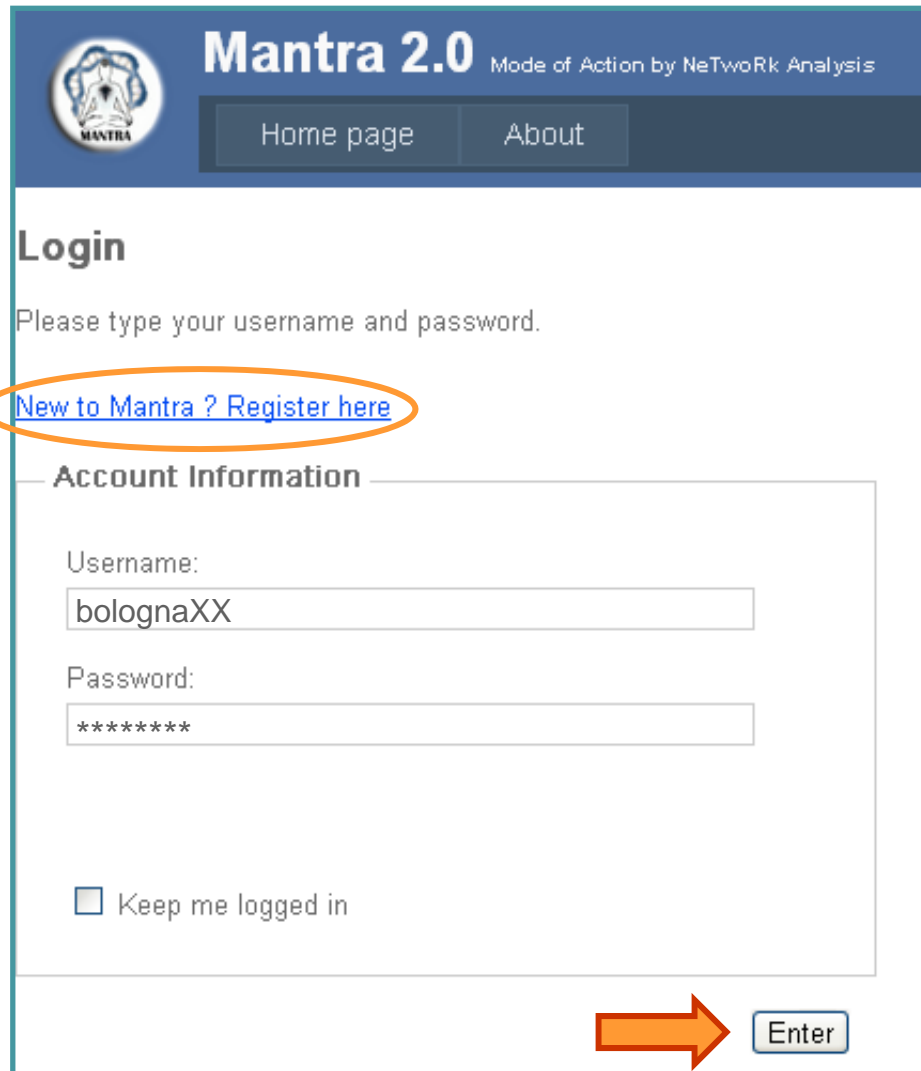
Tools and Informations

The MANTRA analysis framework is implemented as a set of MATLAB functions. The online version of MANTRA has been integrated in a customized version of the [MEDUSA](#) visualization system (a front-end to the [STRING](#) protein interaction database).

Contributors

MANTRA is maintained by [di Bernardo](#) Lab members at TeleThon Institute of Genetics and Medicine ([TIGEM](#)). MANTRA has been developed by Francesco Iorio. The method has been conceived by Francesco Iorio and [Diego di Bernardo](#).



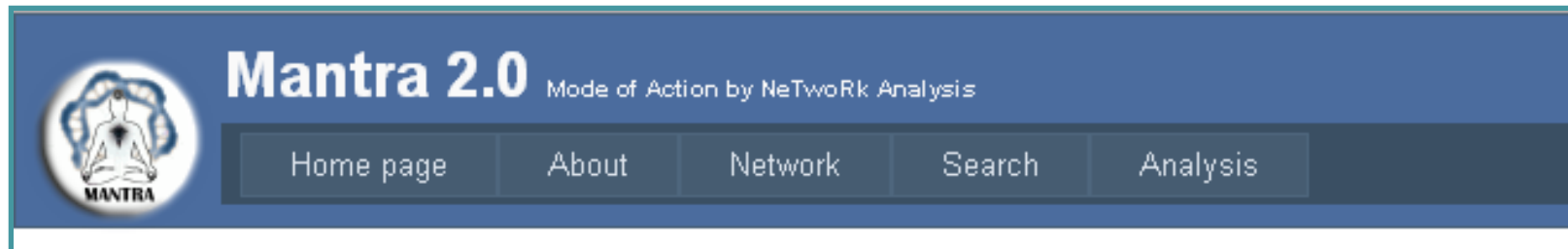
The screenshot shows the Mantra 2.0 web interface. At the top left is the igem logo. The header contains the text "Mantra 2.0 Mode of Action by NeTwoRk Analysis" and navigation links for "Home page" and "About". Below the header is a "Login" section with the instruction "Please type your username and password." A blue link "New to Mantra ? Register here" is circled in orange. Below this is an "Account Information" form with fields for "Username:" (containing "bolognaXX") and "Password:" (containing "*****"). There is a checkbox for "Keep me logged in" which is unchecked. At the bottom right of the form is an "Enter" button, which is highlighted with a large orange arrow pointing to it.

1. If you are not registered, click on **“New to Mantra ? Register here”**;
2. After filling in the registration form, you will receive an email with a link to activate your account;
3. Access to the web tool with your username and password;
4. At last, click on **“Enter”**.

Our web tool consists of three different workspaces:

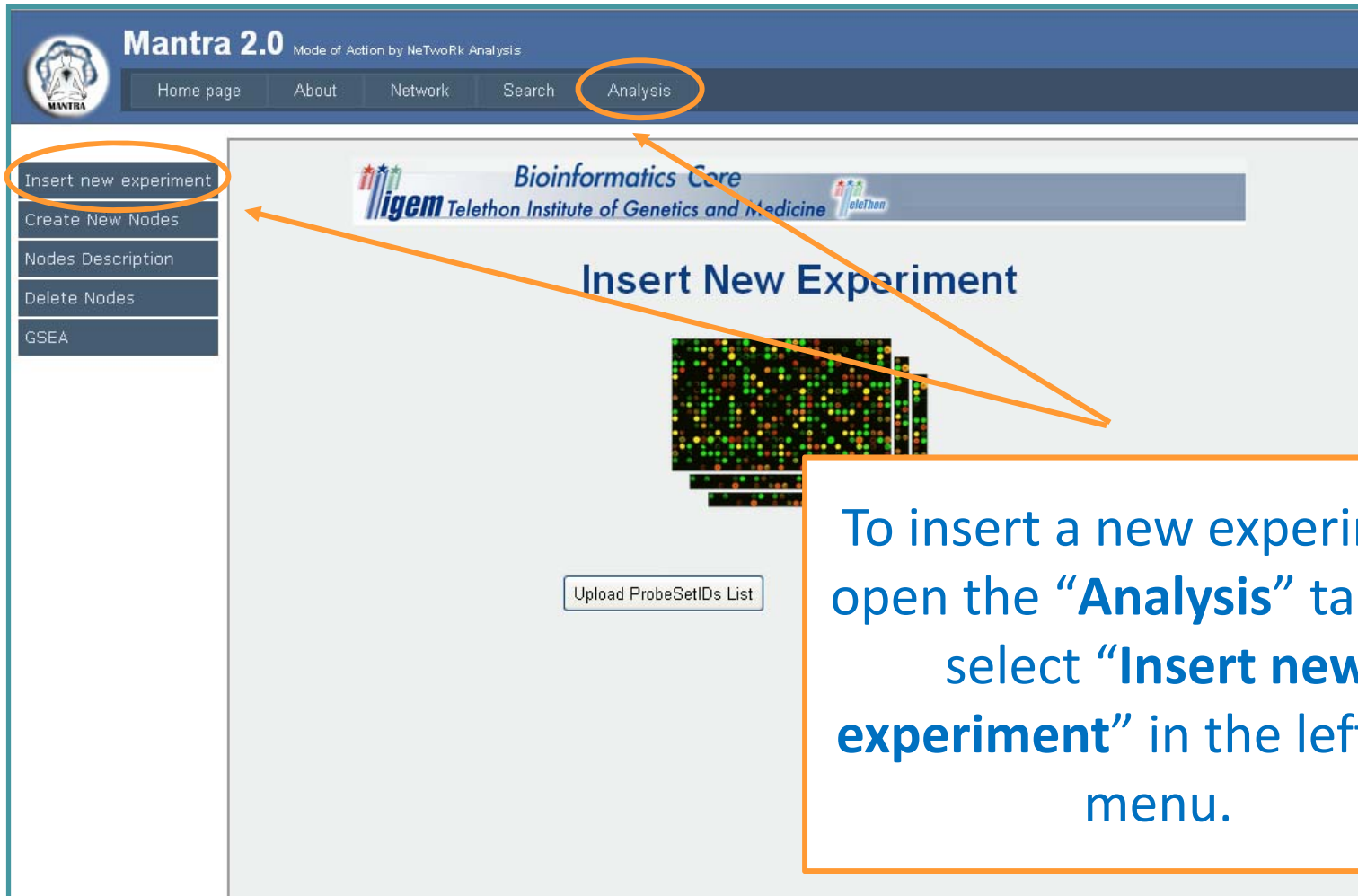
- a) Analysis
- b) Network
- c) Search

Each of these workspaces can be selected, after login, by clicking on the respective tab.



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A user can choose to integrate its own drug in the Network and to classify its MoA by uploading ranked lists of Affymetrix probes or raw data of Affymetrix chips on our server.



The screenshot displays the Mantra 2.0 web interface. The top navigation bar includes the Mantra logo, the title "Mantra 2.0 Mode of Action by NeTwoRk Analysis", and a menu with "Home page", "About", "Network", "Search", and "Analysis". The "Analysis" tab is highlighted with an orange circle. On the left side, a vertical menu contains "Insert new experiment", "Create New Nodes", "Nodes Description", "Delete Nodes", and "GSEA". The "Insert new experiment" item is also highlighted with an orange circle. The main content area features the "Bioinformatics Core" logo, the "igem Telethon Institute of Genetics and Medicine" logo, and the heading "Insert New Experiment". Below this heading is a colorful microarray image and a button labeled "Upload ProbeSetIDs List". A text box on the right provides instructions: "To insert a new experiment open the 'Analysis' tab and select 'Insert new experiment' in the left side menu." Orange arrows point from the text box to the "Analysis" tab and the "Insert new experiment" menu item.

Mantra 2.0 Mode of Action by NeTwoRk Analysis

Home page About Network Search Analysis

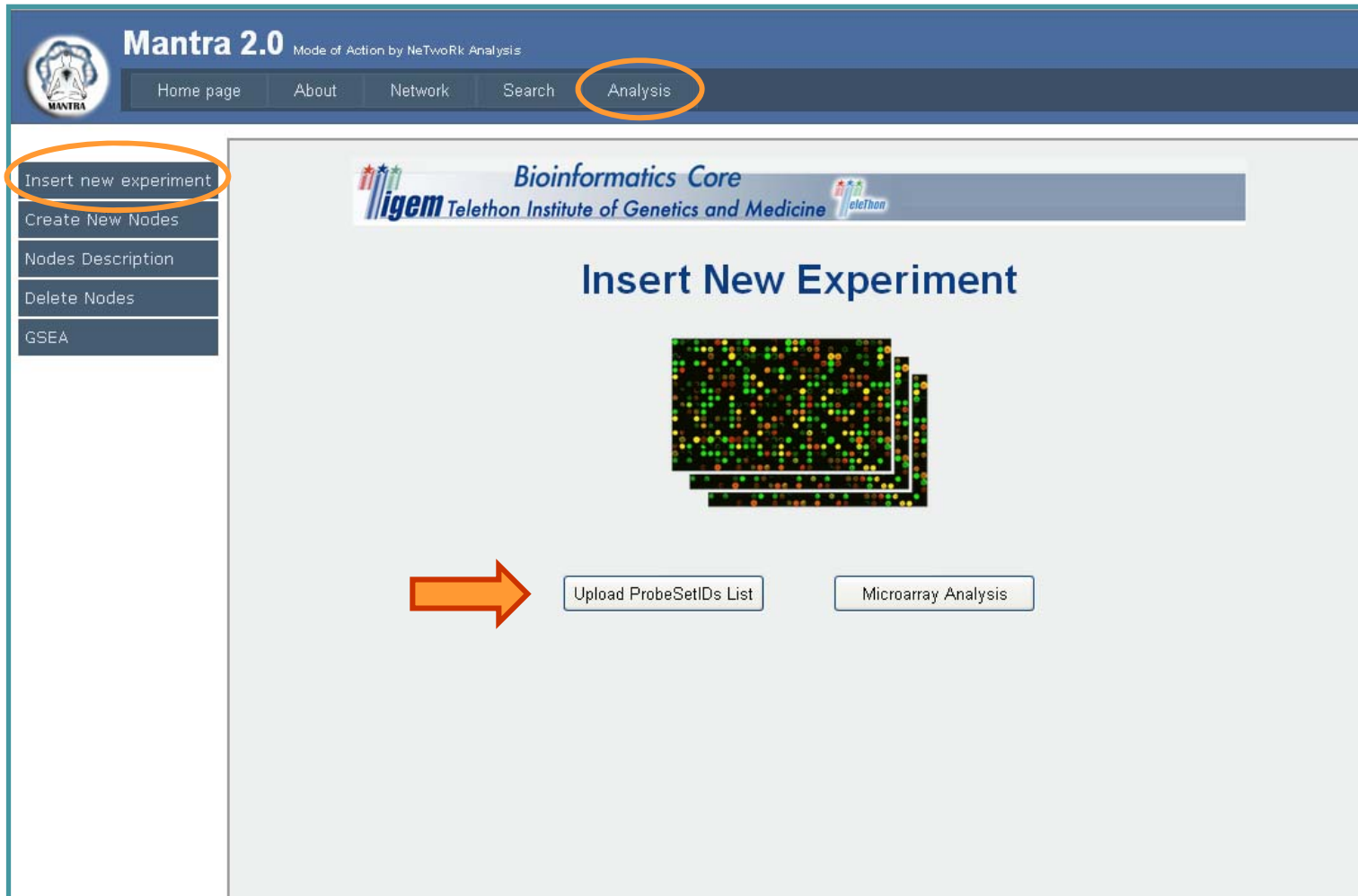
igem Telethon Institute of Genetics and Medicine

Insert New Experiment

Upload ProbeSetIDs List

To insert a new experiment open the "Analysis" tab and select "Insert new experiment" in the left side menu.

To upload a probes list click on “**Upload ProbeSetIDs List**” button.



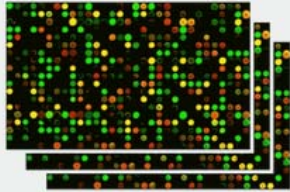
Mantra 2.0 Mode of Action by NeTwoRk Analysis

Home page About Network Search **Analysis**

Insert new experiment
Create New Nodes
Nodes Description
Delete Nodes
GSEA

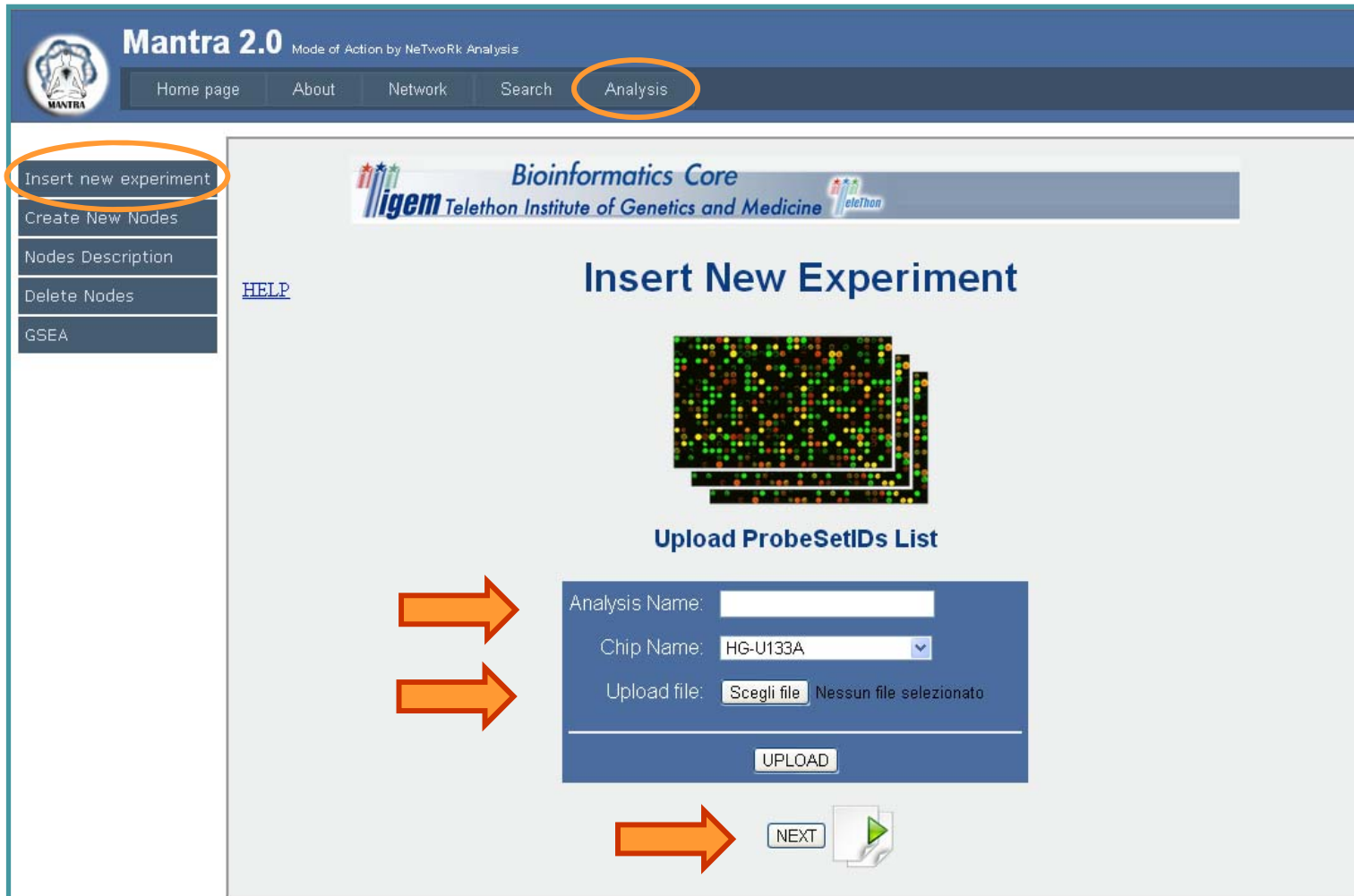
Bioinformatics Core
igem Telethon Institute of Genetics and Medicine telethon

Insert New Experiment



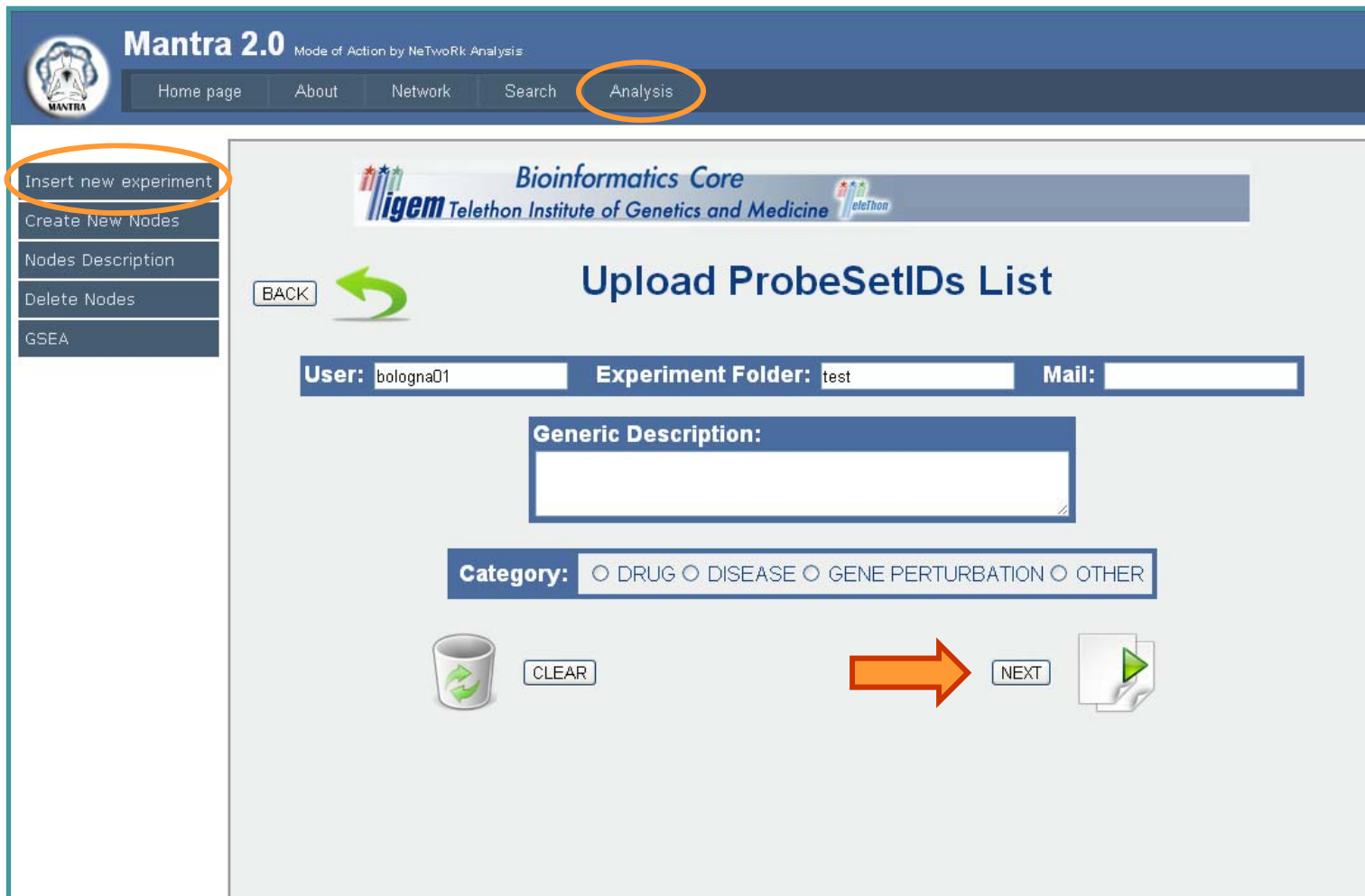
Upload ProbeSetIDs List **Microarray Analysis**

Enter “Analysis Name”, “Chip Name” and select a .txt file, containing all the affymetrix probe-set identifiers sorted according to their differential expression following treatment with the testing drug.



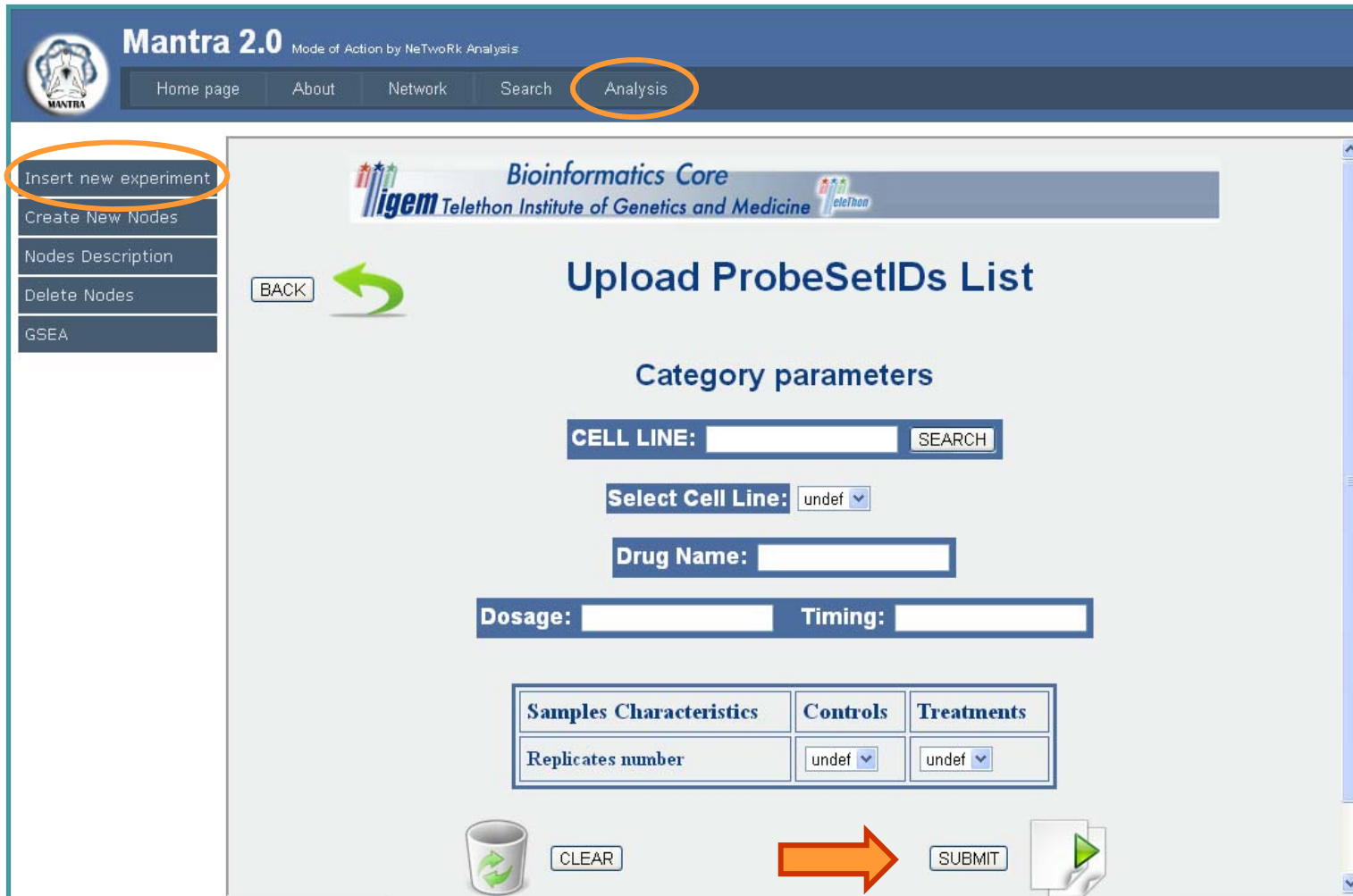
The screenshot displays the Mantra 2.0 web interface. The top navigation bar includes 'Home page', 'About', 'Network', 'Search', and 'Analysis' (circled in orange). The left sidebar contains 'Insert new experiment' (circled in orange), 'Create New Nodes', 'Nodes Description', 'Delete Nodes', and 'GSEA'. The main content area features the 'Bioinformatics Core' header and the 'Insert New Experiment' form. The form includes a 'HELP' link, a 'Upload ProbeSetIDs List' section with a heatmap image, and input fields for 'Analysis Name', 'Chip Name' (set to 'HG-U133A'), and 'Upload file' (with a 'Scegli file' button and 'Nessun file selezionato' text). An 'UPLOAD' button is located below the form. At the bottom, there is a 'NEXT' button and a document icon with a green arrow, both indicated by orange arrows.

Fill some required fields (such as Mail, Generic Description and Category) and click on “NEXT”.



The screenshot shows the Mantra 2.0 web interface. The top navigation bar includes 'Home page', 'About', 'Network', 'Search', and 'Analysis' (circled in orange). The left sidebar contains 'Insert new experiment' (circled in orange), 'Create New Nodes', 'Nodes Description', 'Delete Nodes', and 'GSEA'. The main content area is titled 'Upload ProbeSetIDs List' and features a 'BACK' button with a green arrow. Below this are three input fields: 'User: bologna01', 'Experiment Folder: test', and 'Mail:'. A 'Generic Description:' text area is positioned below these fields. The 'Category:' section includes radio buttons for 'DRUG', 'DISEASE', 'GENE PERTURBATION', and 'OTHER'. At the bottom, there is a 'CLEAR' button with a trash icon, a large orange arrow pointing right, a 'NEXT' button, and a document icon with a green arrow.

Fill some category parameters (such as Cell line, Name, Dosage and Timing, Perturbation Type and Replicates Number) and click on “SUBMIT”.



The screenshot shows the Mantra 2.0 web interface. The top navigation bar includes 'Home page', 'About', 'Network', 'Search', and 'Analysis' (circled in orange). The left sidebar contains 'Insert new experiment' (circled in orange), 'Create New Nodes', 'Nodes Description', 'Delete Nodes', and 'GSEA'. The main content area is titled 'Upload ProbeSetIDs List' and features a 'Category parameters' section with the following fields: 'CELL LINE:' with a text input and a 'SEARCH' button; 'Select Cell Line:' with a dropdown menu showing 'undef'; 'Drug Name:' with a text input; 'Dosage:' and 'Timing:' with text inputs; and a table with columns 'Samples Characteristics', 'Controls', and 'Treatments'. The 'Replicates number' row shows 'undef' in the 'Controls' and 'Treatments' columns. At the bottom, there is a 'CLEAR' button, a large orange arrow pointing right, and a 'SUBMIT' button next to a green arrow icon.

The addition of a Microarray Analysis pipeline allows to analyze raw data from microarray experiments with the Affymetrix platform. Click on **“Microarray Analysis”** button.



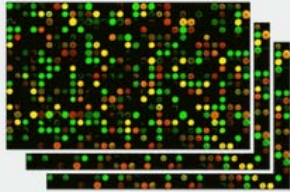
Mantra 2.0 Mode of Action by NeTwoRk Analysis

Home page About Network Search **Analysis**

Insert new experiment
Create New Nodes
Nodes Description
Delete Nodes
GSEA

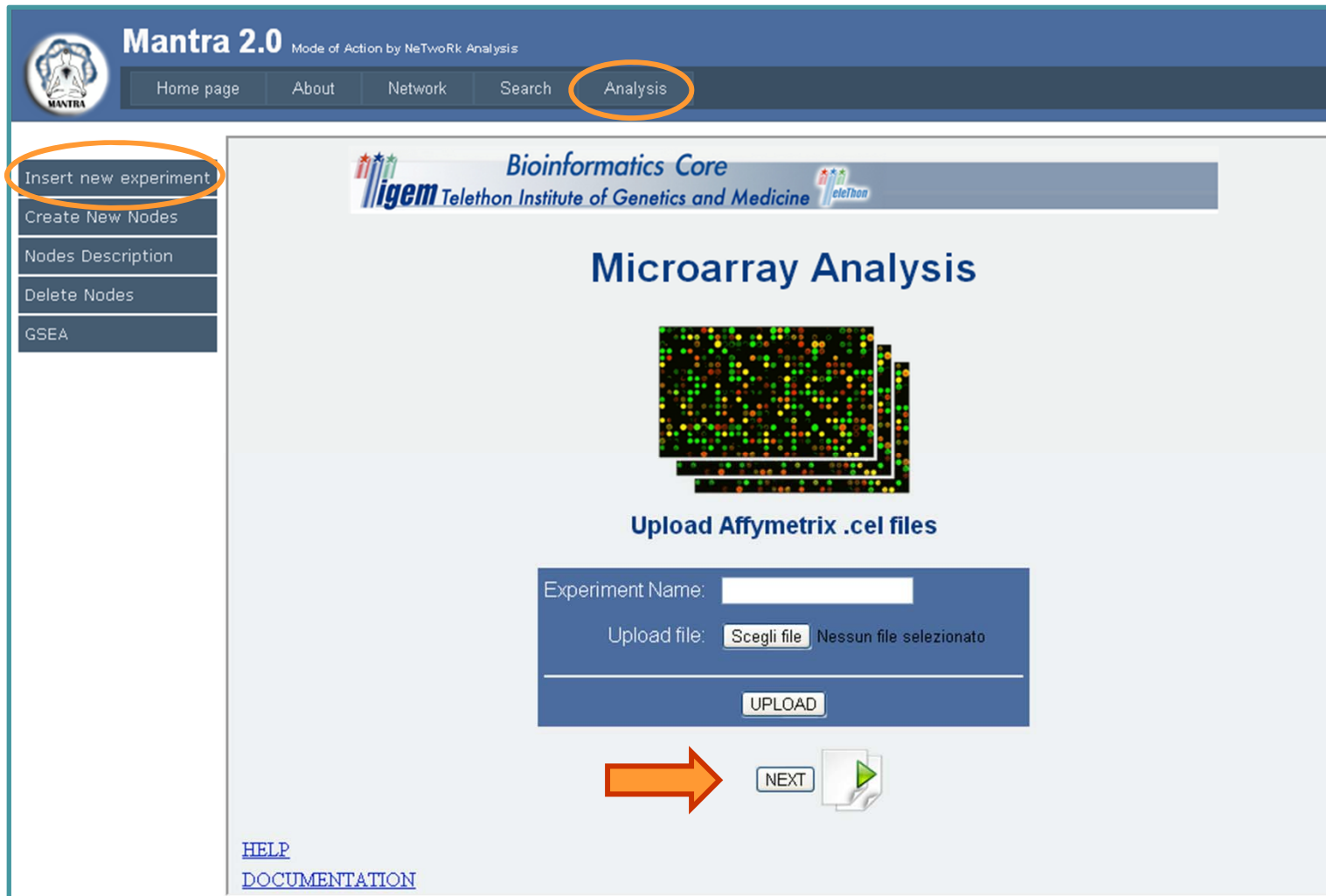
Bioinformatics Core
igem Telethon Institute of Genetics and Medicine telethon

Insert New Experiment



Upload ProbeSetIDs List Microarray Analysis

Upload .cel files and click on “NEXT”.



The screenshot shows the Mantra 2.0 web interface. The top navigation bar includes links for Home page, About, Network, Search, and Analysis (highlighted with an orange circle). The left sidebar contains options: Insert new experiment (highlighted with an orange circle), Create New Nodes, Nodes Description, Delete Nodes, and GSEA. The main content area is titled "Microarray Analysis" and features a colorful microarray image. Below the image, the text "Upload Affymetrix .cel files" is displayed. A form for "Experiment Name" and "Upload file" (with a "Scegli file" button and "Nessun file selezionato" text) is present, followed by an "UPLOAD" button. A large orange arrow points to a "NEXT" button with a green play icon. At the bottom left, there are links for "HELP" and "DOCUMENTATION".

Mantra 2.0 Mode of Action by NeTwoRk Analysis

Home page About Network Search Analysis


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Microarray Analysis

Upload Affymetrix .cel files

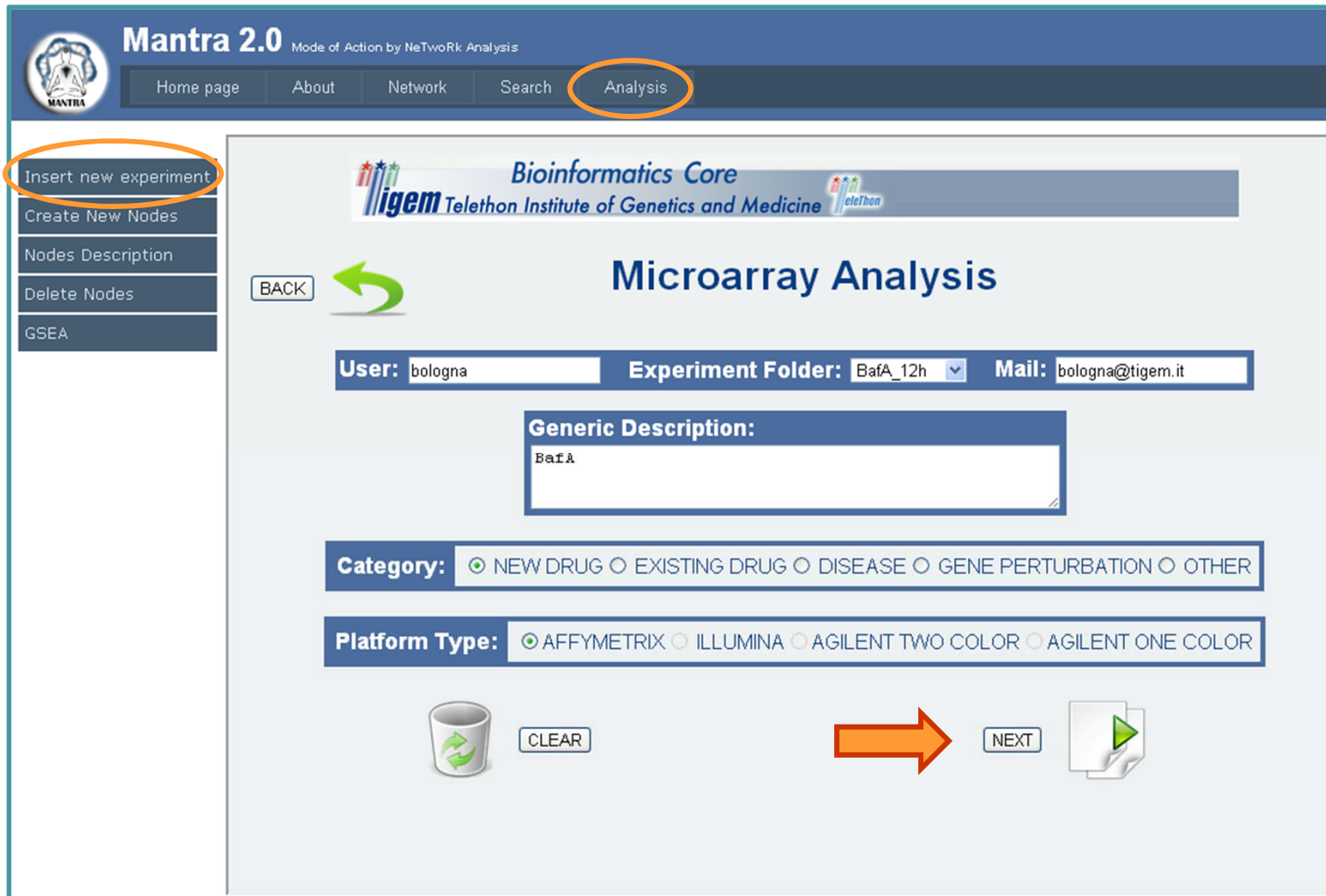
Experiment Name:

Upload file: Nessun file selezionato



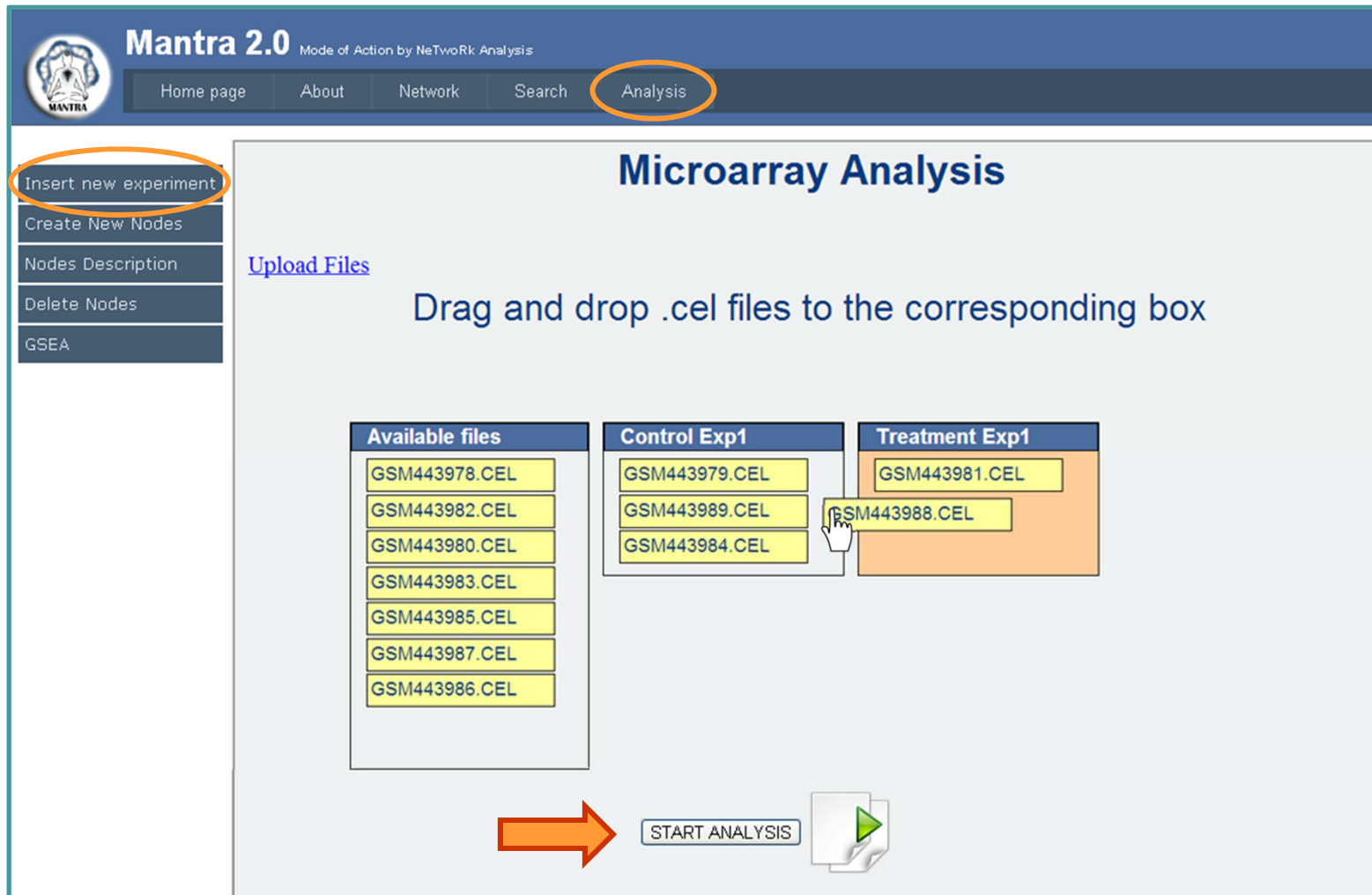
[HELP](#)
[DOCUMENTATION](#)

Fill some required fields (such as Mail, Description, Category and Platform Type) and click on “NEXT”.



The screenshot shows the Mantra 2.0 web interface. The top navigation bar includes links for Home page, About, Network, Search, and Analysis (highlighted with an orange circle). The left sidebar contains a menu with 'Insert new experiment' (highlighted with an orange circle), Create New Nodes, Nodes Description, Delete Nodes, and GSEA. The main content area is titled 'Microarray Analysis' and features a 'BACK' button with a green arrow icon. Below this, there are input fields for 'User: bologna', 'Experiment Folder: BafA_12h', and 'Mail: bologna@tigem.it'. A 'Generic Description:' field contains the text 'BafA'. The 'Category:' section has radio buttons for 'NEW DRUG' (selected), 'EXISTING DRUG', 'DISEASE', 'GENE PERTURBATION', and 'OTHER'. The 'Platform Type:' section has radio buttons for 'AFFYMETRIX' (selected), 'ILLUMINA', 'AGILENT TWO COLOR', and 'AGILENT ONE COLOR'. At the bottom, there is a 'CLEAR' button with a trash can icon, a large orange arrow pointing right, and a 'NEXT' button with a document icon.

Select and load the treated and control files (drag & drop .cel files to the corresponding box) and click on “**START ANALYSIS**”.



The screenshot shows the Mantra 2.0 web interface for Microarray Analysis. The top navigation bar includes 'Home page', 'About', 'Network', 'Search', and 'Analysis' (circled in orange). A left sidebar contains 'Insert new experiment' (circled in orange), 'Create New Nodes', 'Nodes Description', 'Delete Nodes', and 'GSEA'. The main content area is titled 'Microarray Analysis' and contains the text 'Upload Files' and 'Drag and drop .cel files to the corresponding box'. Below this, there are three columns: 'Available files' (listing GSM443978.CEL to GSM443986.CEL), 'Control Exp1' (listing GSM443979.CEL, GSM443989.CEL, and GSM443984.CEL), and 'Treatment Exp1' (listing GSM443981.CEL and GSM443988.CEL). A hand icon is shown dragging the GSM443988.CEL file from the 'Available files' column to the 'Treatment Exp1' column. At the bottom, a large orange arrow points to a 'START ANALYSIS' button next to a document icon with a green play button.

Mantra 2.0 Mode of Action by NeTwork Analysis

Home page About Network Search **Analysis**

Microarray Analysis

[Upload Files](#)

Drag and drop .cel files to the corresponding box

Available files	Control Exp1	Treatment Exp1
GSM443978.CEL	GSM443979.CEL	GSM443981.CEL
GSM443982.CEL	GSM443989.CEL	GSM443988.CEL
GSM443980.CEL	GSM443984.CEL	
GSM443983.CEL		
GSM443985.CEL		
GSM443987.CEL		
GSM443986.CEL		

START ANALYSIS




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Selecting from the list the experiments of interest it is possible to extract “K” ordered lists of genes, one for each experiment selected. The “K” lists, appropriately recombined, contribute to the creation of a new node of the drugs network.


Mantra 2.0 Mode of Action by NeTwoRk Analysis

Home page
About
Network
Search
Analysis

Insert new experiment

Create New Nodes

Nodes Description

Delete Nodes

GSEA

GSEA with PValue

User nodes list

DrugName	Description	IdExp	Sorting	Category
CtBP_Colanzi	CtBP Colanzi p	1	Forward	Other
PI3K_Ex20_R	PI3K Breast with DMSO Geod17785	6	Inverse	Other
PI3K_Ex20dms0/inh_F	PI3K Breast DMSO/Inhib Geod17785	8	Forward	Other
PI3K_Ex9_R	PI3K Breast Ex9 Kltreat - HG1.0	34	Inverse	Other
PHA-690509	A2780 treated CDK-509	35	Forward	Other
PHA-848125	A2780 treated CDK-125 and MCF7 treated CDK-125	36,38	Forward	Other
PHA-793887	A2780 treated CDK-887 and MCF7 treated CDK-887	37,42	Forward	Other

New node

All
Select Experiment Category

CDK-125
Select an experiment Select all experiments

User experiments list

Selected	id_exp	name	data_ins	chip_name	category	description	timing	dosage	perturbation	cell_line
<input type="checkbox"/>	36	CDK-125	22/01/2013 12:06:51	HG-U133_Plus_2	Other	Nerviano Medical Sciences (NMS) - A2780 treated CDK-125	unknown	unknown	unknown	A2780
<input checked="" type="checkbox"/>	38	CDK-125	23/01/2013 09:59:03	HG-U133_Plus_2	Other	Nerviano Medical Sciences (NMS) - MCF7 treated CDK-125	unknown	unknown	unknown	MCF7

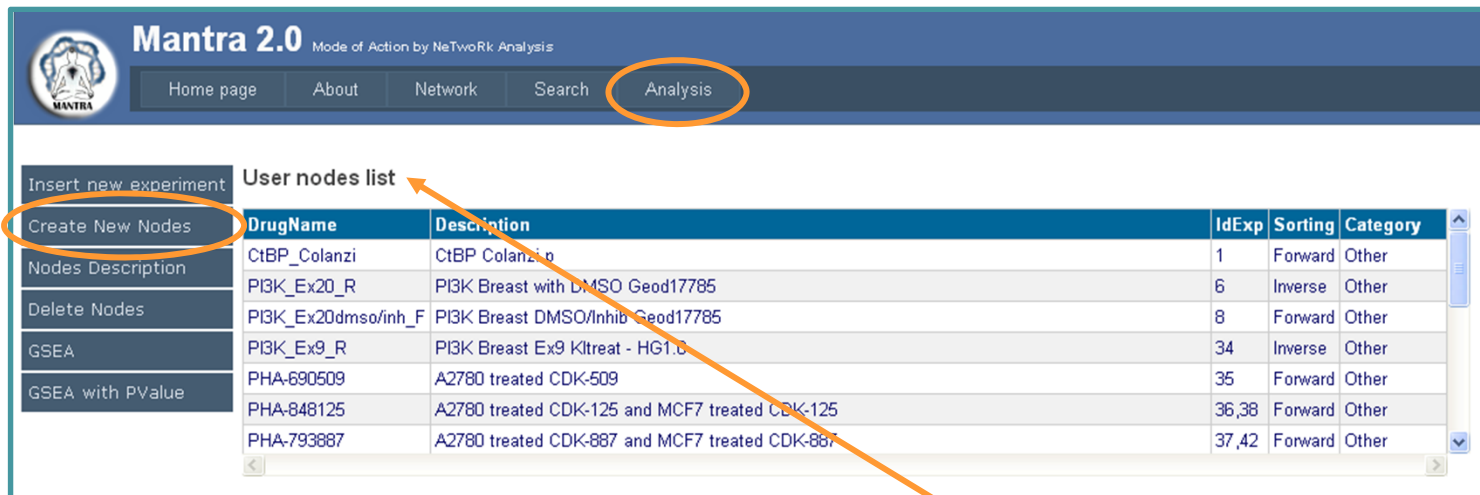
Node name

Node description

Node Category

Is Private

Selecting from the list the experiments of interest it is possible to extract “K” ordered lists of genes, one for each experiment selected. The “K” lists, appropriately recombined, contribute to the creation of a new node of the drugs network.



Mantra 2.0 Mode of Action by NeTwoRk Analysis

Home page About Network Search **Analysis**

Insert new experiment

Create New Nodes

Nodes Description

Delete Nodes

GSEA

GSEA with PValue

User nodes list

DrugName	Description	IdExp	Sorting	Category
CtBP_Colanzi	CtBP Colanzi	1	Forward	Other
PI3K_Ex20_R	PI3K Breast with DMSO Geod17785	6	Inverse	Other
PI3K_Ex20dms0/inh_F	PI3K Breast DMSO/Inhib Geod17785	8	Forward	Other
PI3K_Ex9_R	PI3K Breast Ex9 Kltreat - HG1.0	34	Inverse	Other
PHA-690509	A2780 treated CDK-509	35	Forward	Other
PHA-848125	A2780 treated CDK-125 and MCF7 treated CDK-125	36,38	Forward	Other
PHA-793887	A2780 treated CDK-887 and MCF7 treated CDK-887	37,42	Forward	Other

**Nodes created
by the user**

Selecting from the list the experiments of interest it is possible to extract “K” ordered lists of genes, one for each experiment selected. The “K” lists, appropriately recombined, contribute to the creation of a new node of the drugs network.

Select experiments using the appropriate drop-down menu.
Fill the fields (Name, Description, Category) and click on “**Create Node**” (or “Create Inverse Node”).

“Create Inverse Node”: to create ranked list of genes with inverse sorting.

New node

All Select Experiment Category
 CDK-125 Select an experiment Select all experiments

User experiments list

Selected	id_exp	name	data_ins	chip_name	category	description	timing	dosage	perturbation	cell_line
<input type="checkbox"/>	36	CDK-125	22/01/2013 12:06:51	HG-U133_Plus_2	Other	Nerviano Medical Sciences (NMS) - A2780 treated CDK-125	unknown	unknown	unknown	A2780
<input checked="" type="checkbox"/>	38	CDK-125	23/01/2013 09:59:03	HG-U133_Plus_2	Other	Nerviano Medical Sciences (NMS) - MCF7 treated CDK-125	unknown	unknown	unknown	MCF7

Node name

Node description

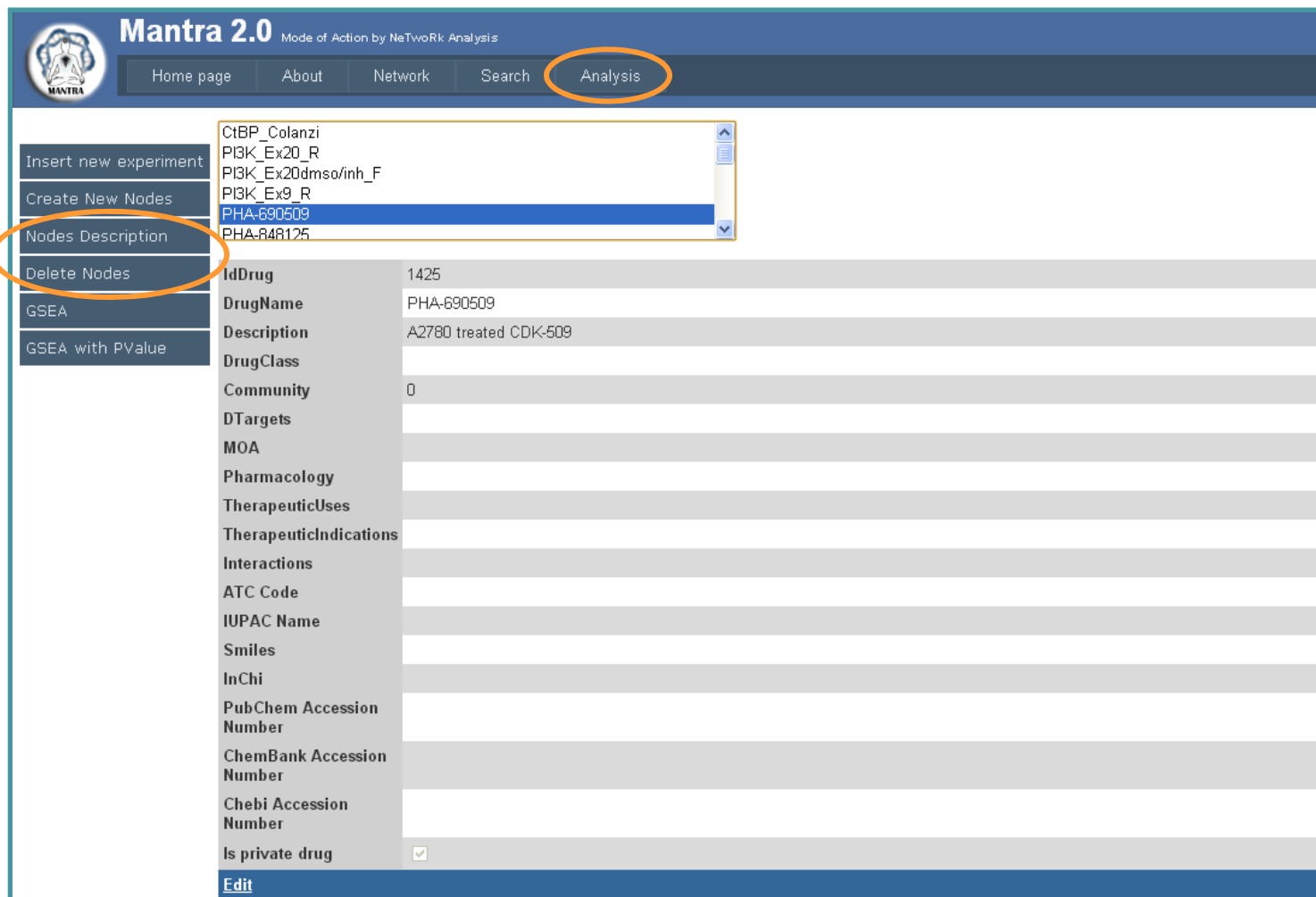
Node Category

Is Private

NEW NODE - Editing and Deleting

Two possible operations on the nodes:

1. annotate and edit the details of the user nodes
2. delete the user nodes



Mantra 2.0 Mode of Action by NeTwoRk Analysis

Home page About Network Search **Analysis**

Insert new experiment
Create New Nodes
Nodes Description
Delete Nodes
GSEA
GSEA with PValue

CtBP_Colanzi
PI3K_Ex20_R
PI3K_Ex20dmso/inh_F
PI3K_Ex9_R
PHA-690509
PHA-848125

IdDrug	1425
DrugName	PHA-690509
Description	A2780 treated CDK-509
DrugClass	
Community	0
DTargets	
MOA	
Pharmacology	
TherapeuticUses	
TherapeuticIndications	
Interactions	
ATC Code	
IUPAC Name	
Smiles	
InChi	
PubChem Accession Number	
ChemBank Accession Number	
Chebi Accession Number	
Is private drug	<input checked="" type="checkbox"/>

[Edit](#)

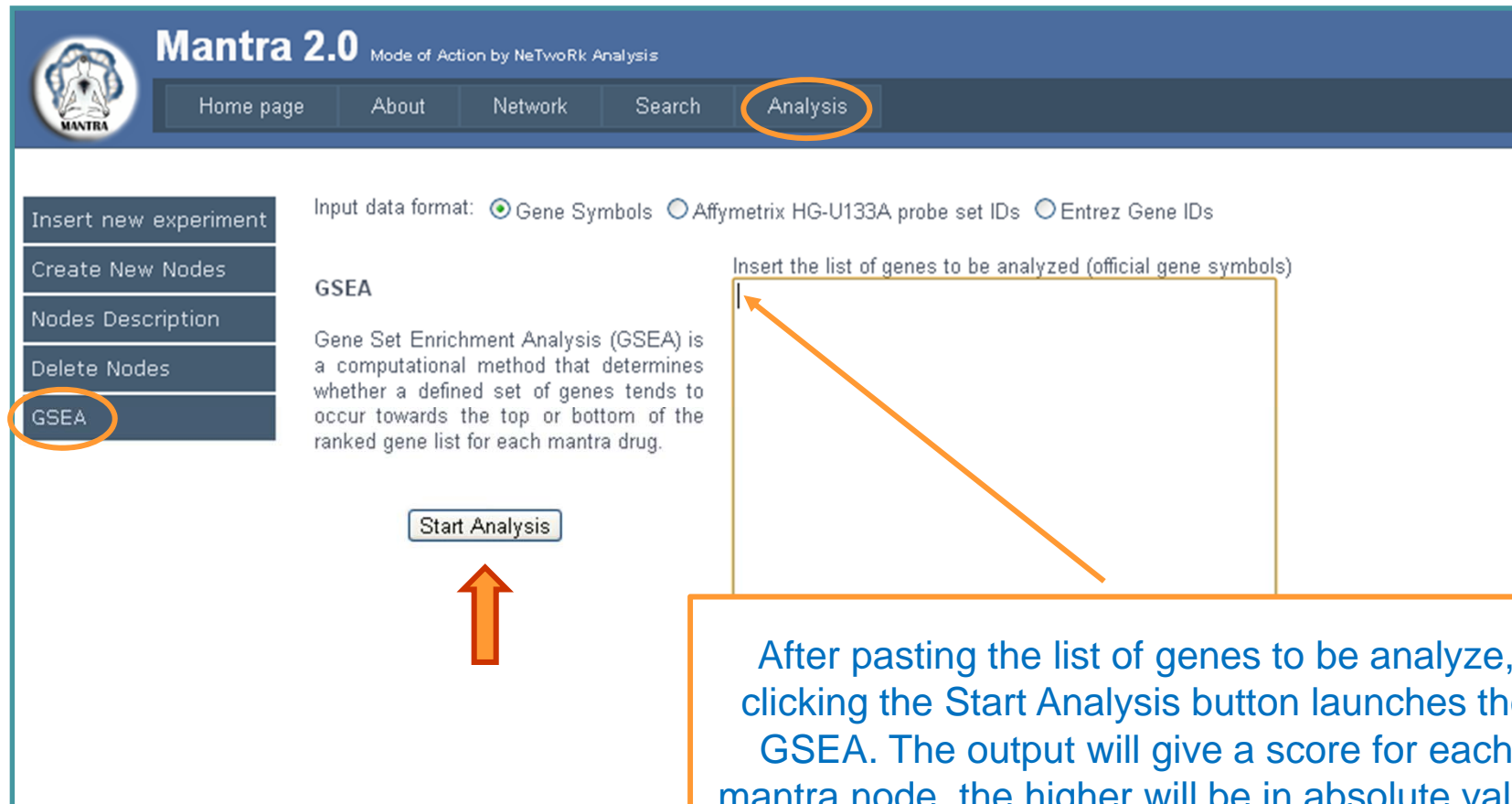


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Gene Set Enrichment Analysis (GSEA) is a computational method that determines whether a defined set of genes tends to occur towards the top or bottom of the ranked gene list for each mantra drug.



The screenshot shows the Mantra 2.0 web interface. The header includes the Mantra logo and the text "Mantra 2.0 Mode of Action by NeTwoRk Analysis". A navigation menu contains "Home page", "About", "Network", "Search", and "Analysis" (circled in orange). On the left, a sidebar menu lists "Insert new experiment", "Create New Nodes", "Nodes Description", "Delete Nodes", and "GSEA" (circled in orange). The main content area has "Input data format:" with radio buttons for "Gene Symbols" (selected), "Affymetrix HG-U133A probe set IDs", and "Entrez Gene IDs". Below this is the "GSEA" section with a description: "Gene Set Enrichment Analysis (GSEA) is a computational method that determines whether a defined set of genes tends to occur towards the top or bottom of the ranked gene list for each mantra drug." To the right is a text input field labeled "Insert the list of genes to be analyzed (official gene symbols)". Below the input field is a "Start Analysis" button. An orange arrow points from the "Start Analysis" button up to the input field. A callout box at the bottom right contains the following text:

After pasting the list of genes to be analyze, clicking the Start Analysis button launches the GSEA. The output will give a score for each mantra node, the higher will be in absolute value the more the set of genes will be enriched.

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The network tab provides a subnet view based on several parameters (distance threshold, the number of neighbors, depth, number max nodes) and according to the selection of one or more nodes available.

Mantra 2.0 Mode of Action by NeTWork Analysis

Home page About **Network** Search Analysis

Update Network Unselect all Check Distance Table Hierarchical Table Common Genes Cytoscape File

Press Shift+ Click on Node for additional informations

Distance Threshold: 0.8

Neighbours: 20

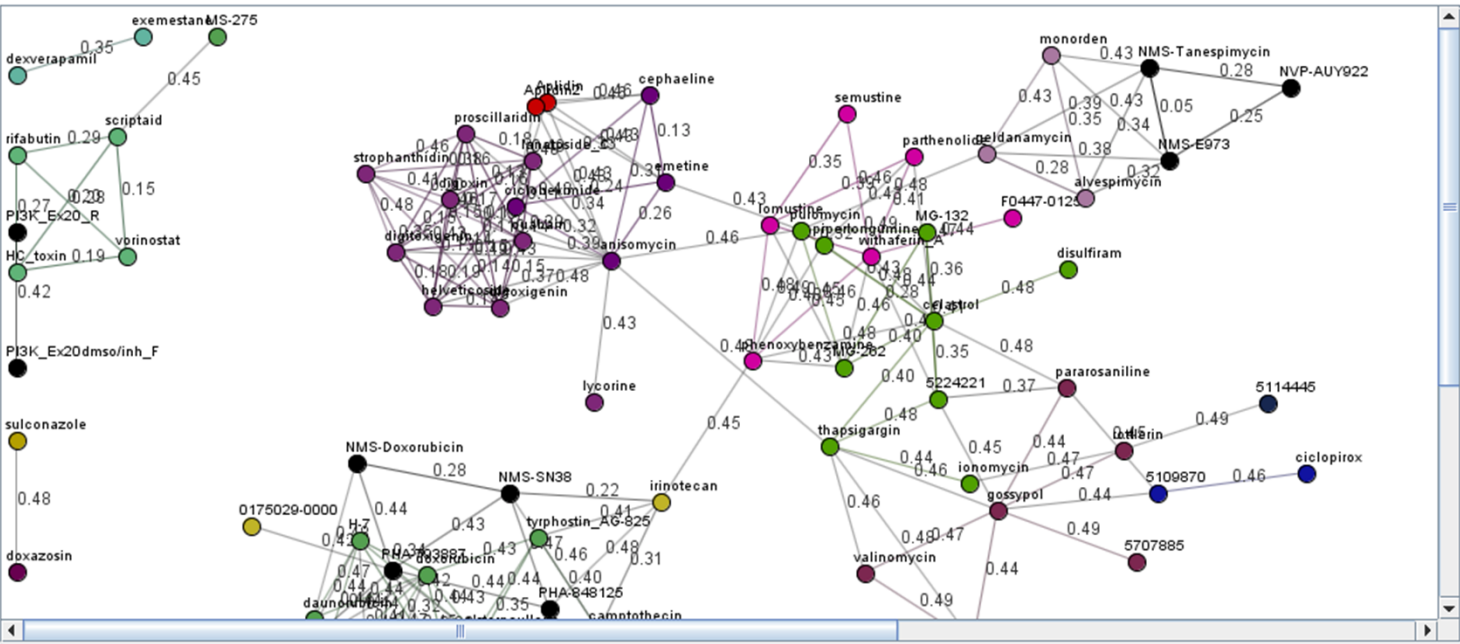
Depth: 1

Max nodes number: 1000

Available nodes: 123

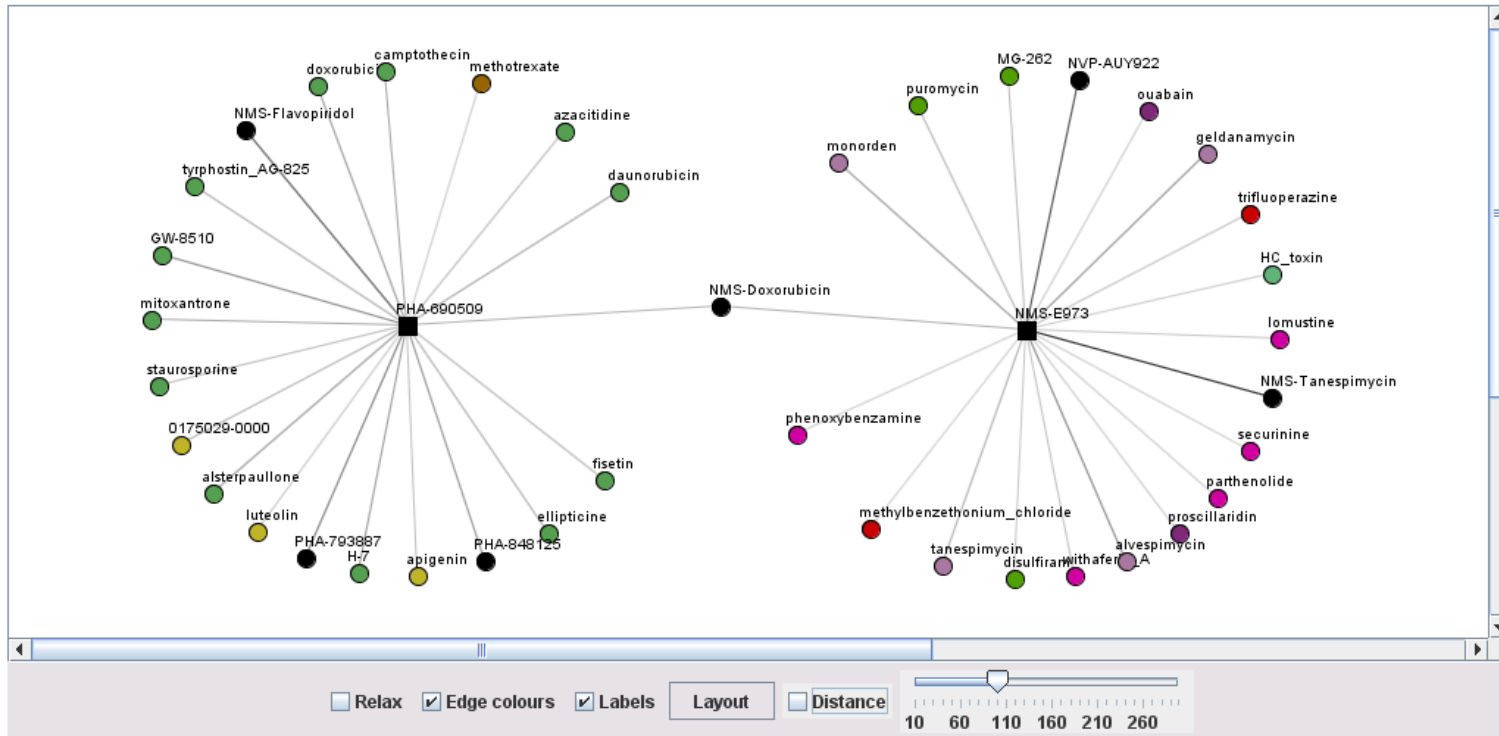
View all Nodes

- Aplidin
- Aplidin2
- CtBP_Colanzi
- ID-del_1
- ID-del_2
- ID-del_3
- NMS-Doxorubicin
- NMS-E973
- NMS-Flavopiridol
- NMS-SN38
- NMS-Tanespimycin
- NVP-AUY922
- PHA-690509
- PHA-793887
- PHA-848125
- PI3K_Ex20dms/inh_F

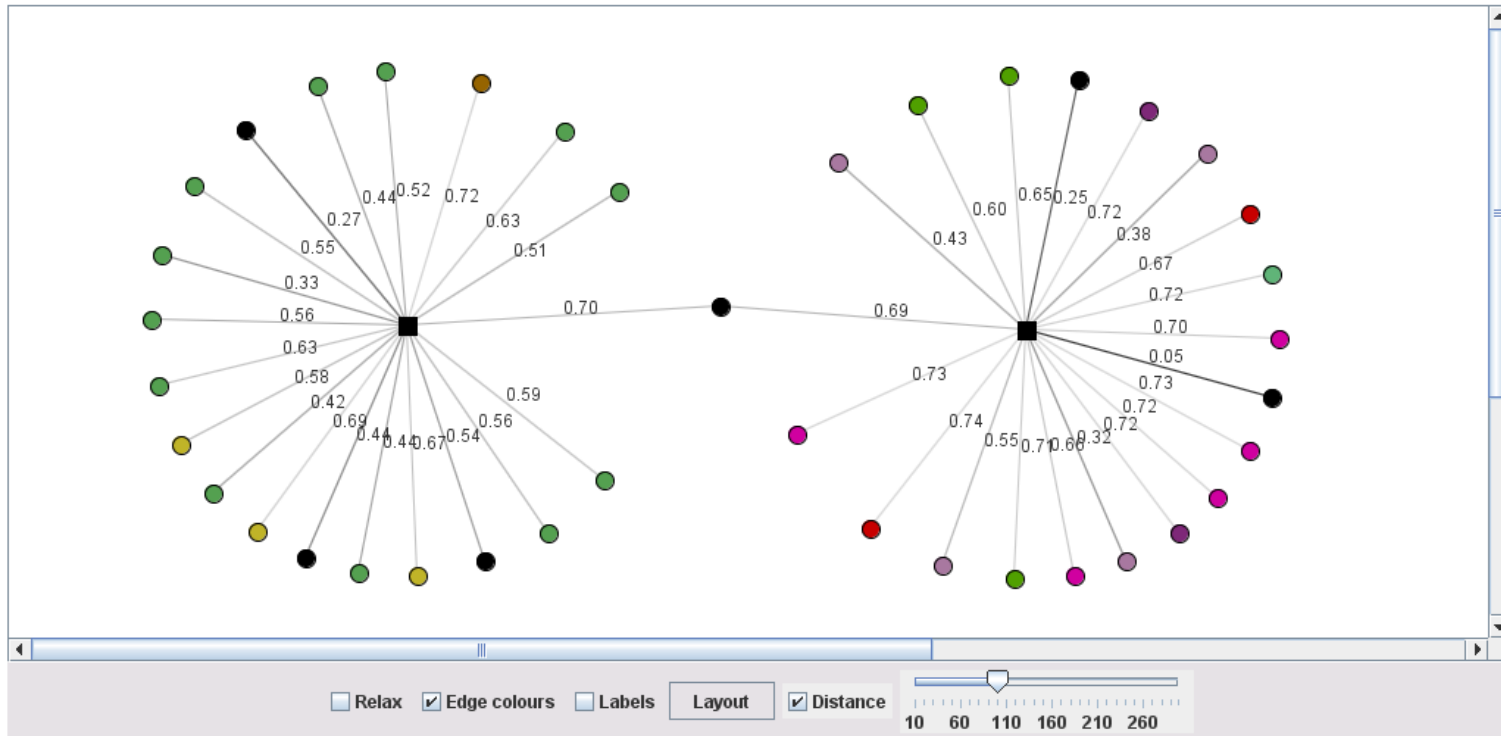


Relax Edge colours Labels Layout Distance

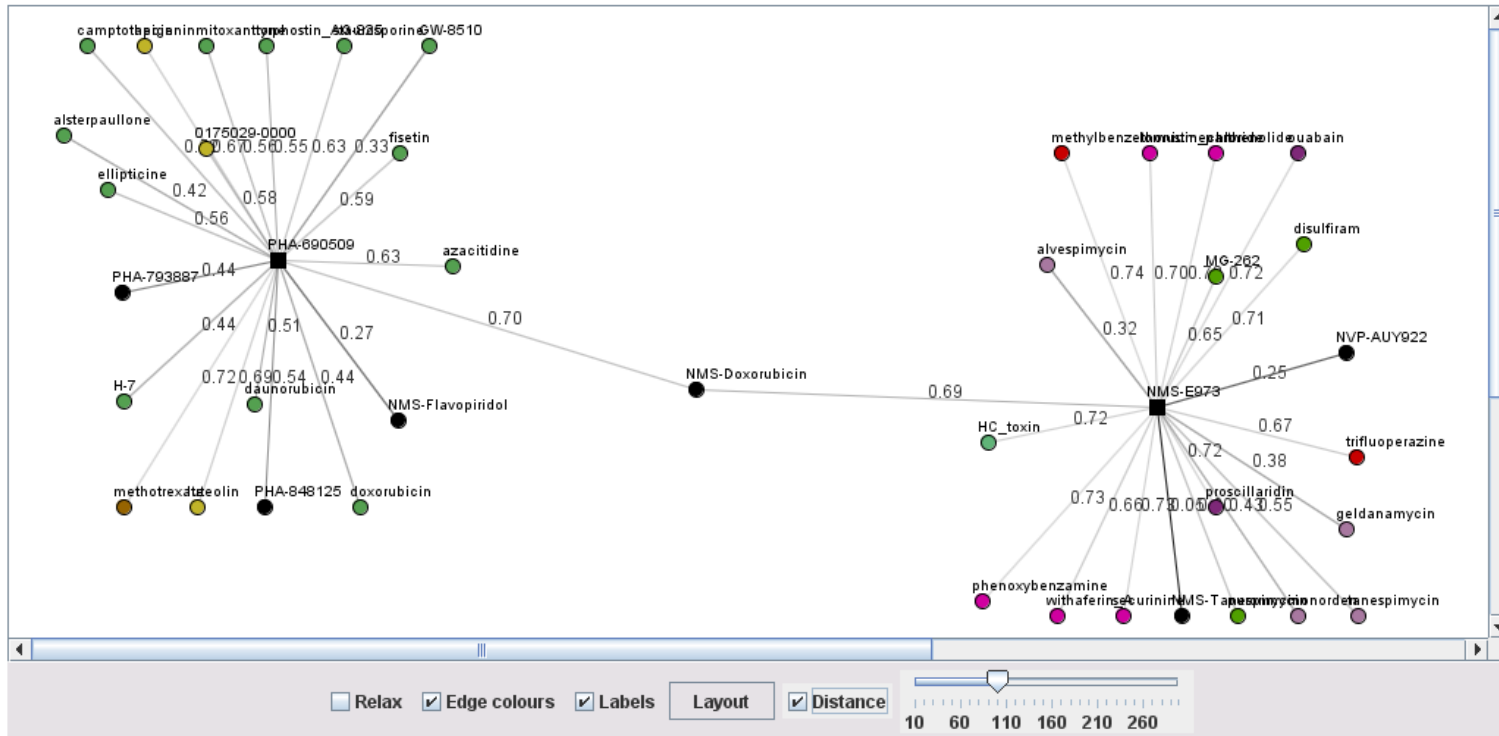
10 60 110 160 210 260



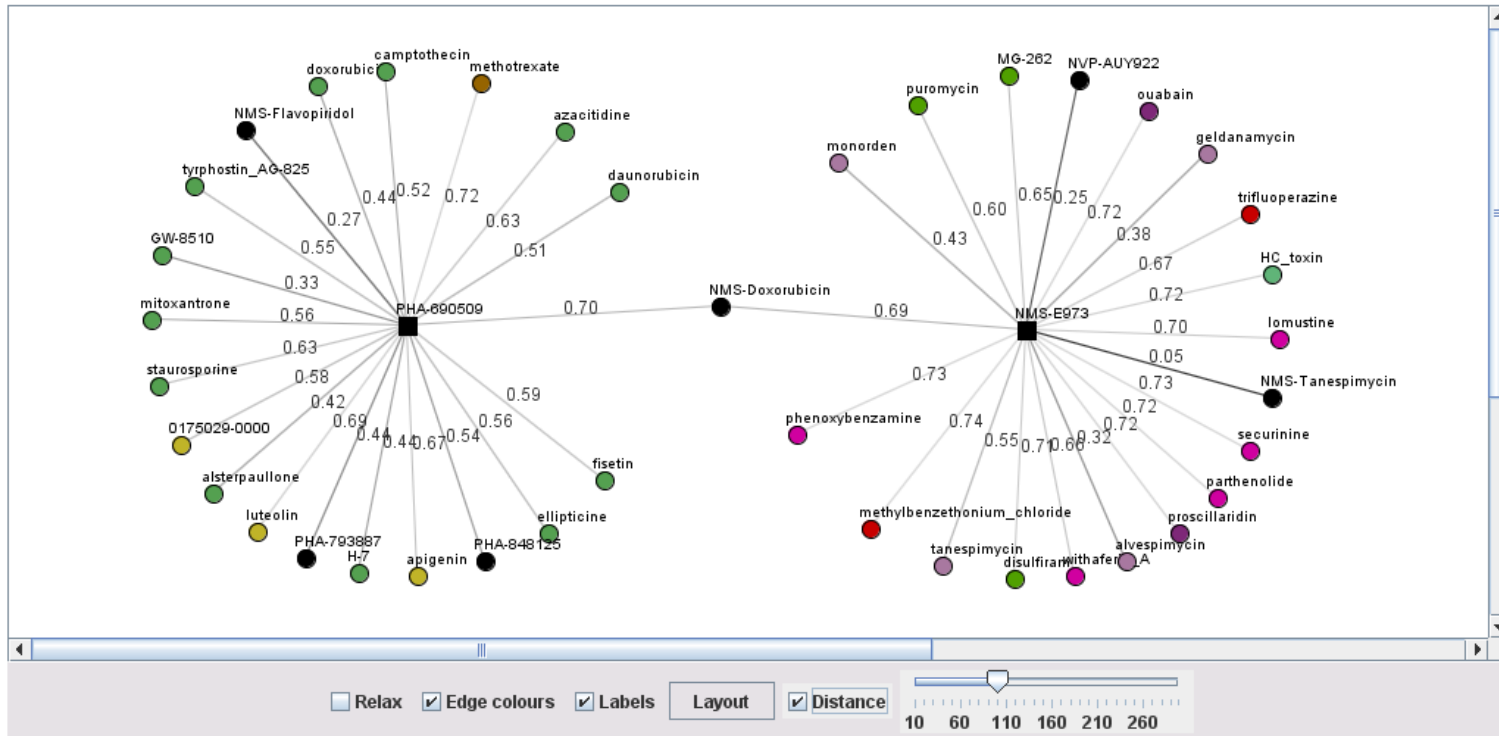
You can unflag “**Distance**” to erase the label of the edges.



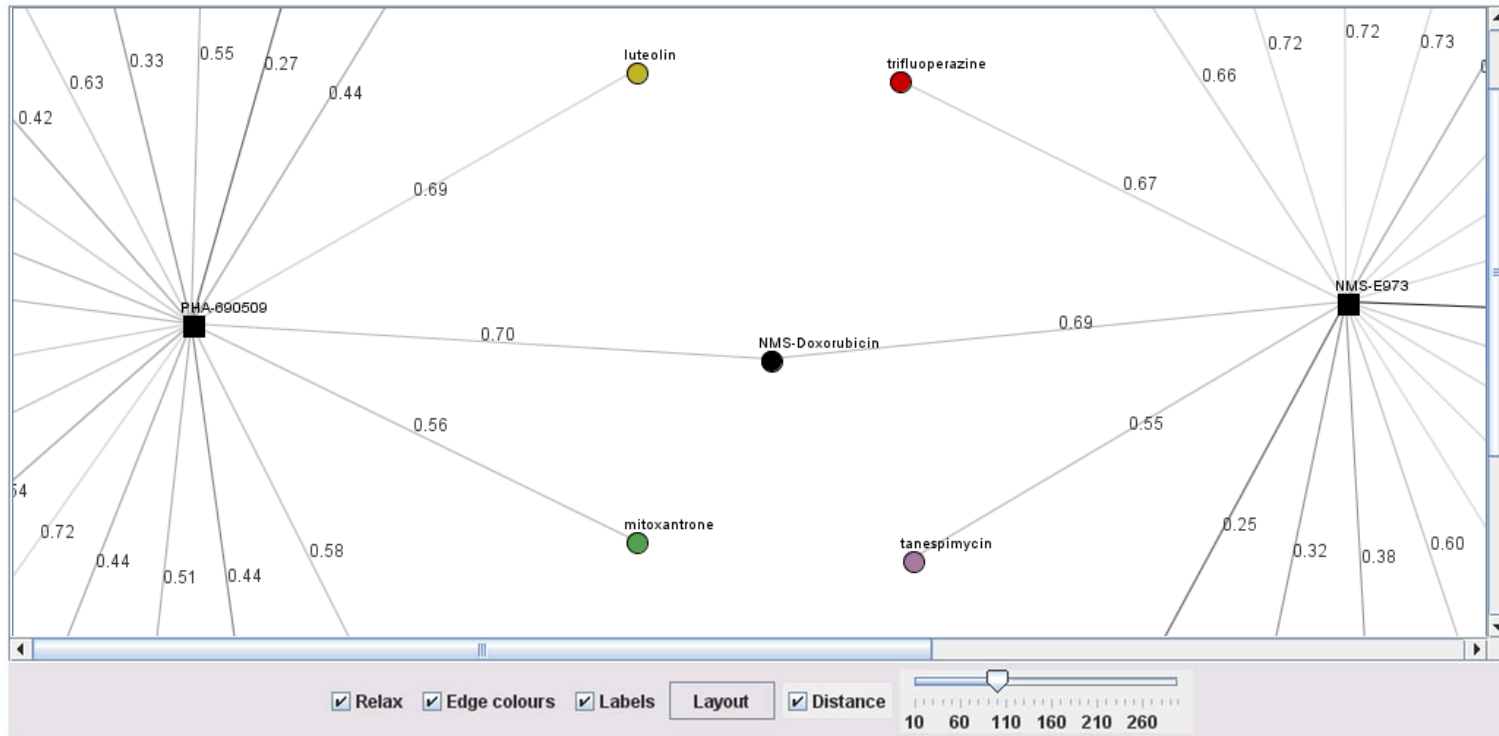
You can unflag “**Labels**” to erase the label of the nodes.



You can click on “**Layout**” to change the network topology.



You can flag “Relax” to relax the network edges.

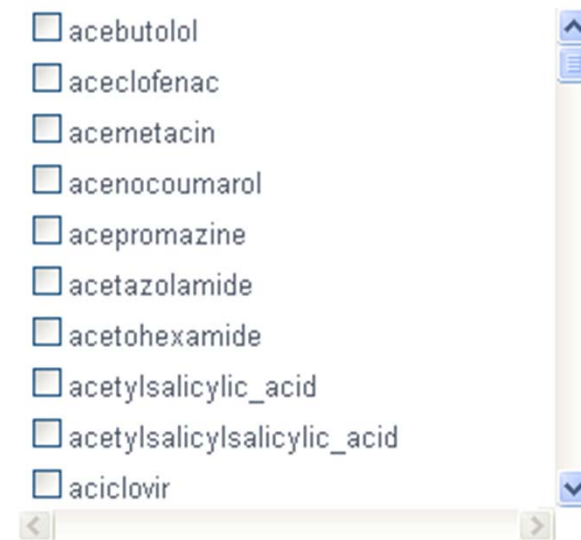


You can move the **sliding bar** to zoom in a part of the network.

From the left side menu you can edit the search parameters to browse the network

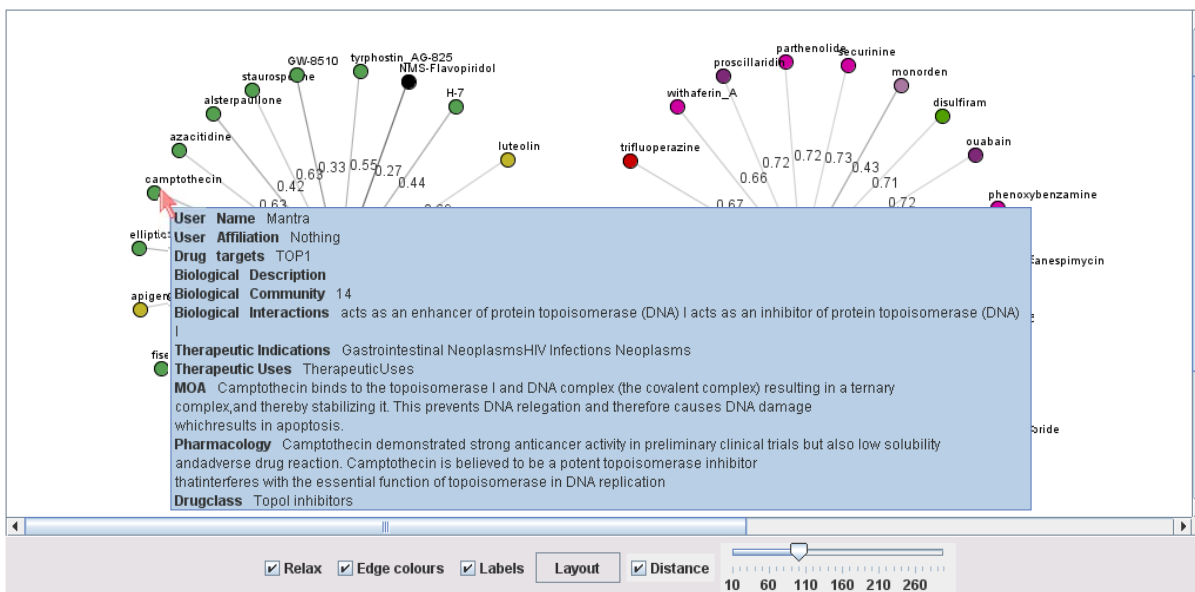
Distance Threshold:	<input type="text" value="0.8"/>	← Threshold to filter the network based on the edges distance
Neighbours:	<input type="text" value="100"/>	← Number of nodes by visualize near at the selected node
Depth:	<input type="text" value="1"/>	← Level of network navigation
Max nodes number	<input type="text" value="1000"/>	← Max number of nodes visualizable
Available nodes:	<input type="text" value="12"/>	← Displayed nodes; nodes available on the applet
View all Nodes	<input checked="" type="checkbox"/>	← Flag to view the entire nodes list or personal nodes only

Available nodes that could be used as targets of network exploration



To visualize the nodes information :

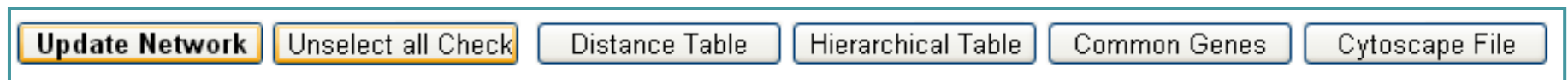
1. hover the mouse on a node to open a tooltip
2. press shift + click on node to open an additional information page, with links to external drug databases



idDrugs	1064
DrugName	puromycin
DrugClass	protein synthesis inhibitors (elongation inhibitors)
Community	40
DTargets	
Interactions	
TherapeuticIndications	
TherapeuticUses	
MOA	
Pharmacology	
x	0.5
y	0.5
c	0,255,0
ATC_Code	
IUPAC_Name	3'-((2S)-2-azaniumyl-3-(4-methoxyphenyl)propanoyl)amino}-3'-deoxy-N,N-dimethyladenosine
Smiles	COc1ccc(C[C@H]([NH3+])C(=O)N[C@@H]2[C@@H]([CO]O[C@H]([C@@H]2O)n2cnc3c(ncnc23)N(C)C)cc1
InChi	InChi=1S/C22H29N7O5/c1-28(2)19-17-20(25-10-24-19)29(11-26-17)22-18(31)16(15(9-30)34-22)27-21(32)14(23)8-12-4-6-13(33-3)7-5-12/h4-7,10-11,14-16,18,22,30-31H,8-9,23H2,1-3H3,(H,27,32)/p+1/t14-,15+,16+,18+,22+/m0/s1
PubChemAccessionNumber	99364948
ChemBankAccessionNumber	
ChebiAccessionNumber	60255

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In the top panel there are six buttons, each with a specific function. The first two buttons can be used to change the displayed network.



Update Network

update the network in basis
to selected parameters in the
navigation menu and to
selected nodes

Unselect all Check

refresh the network
unselecting all nodes



Selected Drug	Distance	Drug2	Community	Description	TherapeuticIndications	Interactions	Drugclass
NMS-E973	0	NMS-E973	0	MCF7 treated E973			
NMS-E973	0,0571304	NMS-Tanespimycin	0	MCF7 treated Tanespimycin-17AAG			
NMS-E973	0,25499	NVP-AUY922	0	MCF7 treated AUY922			
NMS-E973	0,324595	alvespimycin	28				HSP9- inhibitors
NMS-E973	0,388934	geldanamycin	28		Gram-Negative Bacterial InfectionsProtozoan Infections Gram-Positive Bacterial	acts as an inhibitor of protein heat shock protein 90kDa alpha	HSP9- inhibitors
NMS-E973	0,433366	monorden	28			acts as an inhibitor of protein v-src sarcoma (Schmidt-Ruppin A-2) viral	HSP9- inhibitors
NMS-E973	0,556559	tanespimycin	28				HSP9- inhibitors
NMS-E973	0,604252	puromycin	40				protein synthesis inhibitors (elongation)
NMS-E973	0,651395	MG-262	40				Proteasome inhibitors and UPS
NMS-E973	0,666335	withaferin_A	104				-
NMS-E973	0,673863	trifluoperazine	100		Vomiting	acts as an antagonist of protein dopamine receptor D2	Antipsychotics (Phenothiazines)
NMS-E973	0,695055	NMS-Doxorubicin	0	MCF7 treated Doxorubicin			
NMS-E973	0,708295	lomustine	104				nitrosoarea compounds used as

This table contains the distances of displayed edges and the details of nodes near to selected nodes (such as Community, Description, Therapeutic Indications, Interactions, Drug Class, etc.).

[Update Network](#)
[Unselect all Check](#)
[Distance Table](#)
[Hierarchical Table](#)
[Common Genes](#)
[Cytoscape File](#)



This table contains a hierarchical structure in basis to the connections.

Clicking on a name you can visualize the node information in a right window.

NMS-SN38	NMS-E973 - 0.7882506	NMS-Tanespimycin - 0.0571304	NMS-E973 - 0.0571304	<table border="1"> <tr><td>idDrugs</td><td>630</td></tr> <tr><td>DrugName</td><td>geldanamycin</td></tr> <tr><td>DrugClass</td><td>HSP9- inhibitors</td></tr> <tr><td>Community</td><td>28</td></tr> <tr><td>DTargets</td><td>HSP90AA1, HSP62</td></tr> <tr><td>Interactions</td><td>acts as an inhibitor of protein heat shock protein 90kDa alpha (cytosolic), class A member 1 acts as an inhibitor of protein heat shock protein 90kDa alpha (cytosolic), class A member 1</td></tr> <tr><td>TherapeuticIndications</td><td>Gram-Negative Bacterial InfectionsProtozoan Infections Gram-Positive Bacterial InfectionsMycoses Neoplasms</td></tr> <tr><td>TherapeuticUses</td><td></td></tr> <tr><td>MOA</td><td></td></tr> <tr><td>Pharmacology</td><td></td></tr> <tr><td>x</td><td>0.5</td></tr> <tr><td>y</td><td>0.5</td></tr> <tr><td>c</td><td>0,255,0</td></tr> <tr><td>ATC_Code</td><td></td></tr> <tr><td>IUPAC_Name</td><td></td></tr> <tr><td>Smiles</td><td></td></tr> <tr><td>InChi</td><td></td></tr> <tr><td>PubChemAccessionNumber</td><td></td></tr> <tr><td>ChemBankAccessionNumber</td><td></td></tr> </table>	idDrugs	630	DrugName	geldanamycin	DrugClass	HSP9- inhibitors	Community	28	DTargets	HSP90AA1, HSP62	Interactions	acts as an inhibitor of protein heat shock protein 90kDa alpha (cytosolic), class A member 1 acts as an inhibitor of protein heat shock protein 90kDa alpha (cytosolic), class A member 1	TherapeuticIndications	Gram-Negative Bacterial InfectionsProtozoan Infections Gram-Positive Bacterial InfectionsMycoses Neoplasms	TherapeuticUses		MOA		Pharmacology		x	0.5	y	0.5	c	0,255,0	ATC_Code		IUPAC_Name		Smiles		InChi		PubChemAccessionNumber		ChemBankAccessionNumber	
idDrugs	630																																									
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TherapeuticIndications	Gram-Negative Bacterial InfectionsProtozoan Infections Gram-Positive Bacterial InfectionsMycoses Neoplasms																																									
TherapeuticUses																																										
MOA																																										
Pharmacology																																										
x	0.5																																									
y	0.5																																									
c	0,255,0																																									
ATC_Code																																										
IUPAC_Name																																										
Smiles																																										
InChi																																										
PubChemAccessionNumber																																										
ChemBankAccessionNumber																																										
		NMS-SN38 - 0.788472	NMS-SN38 - 0.788472																																							
		NVP-AUY922 - 0.2549896	NMS-E973 - 0.2549896																																							
		alvespimycin - 0.3245948	NMS-E973 - 0.3245948																																							
		geldanamycin - 0.3889336	NMS-E973 - 0.3889336																																							
		monorden - 0.433366	NMS-E973 - 0.433366																																							
		tanespimycin - 0.556559	NMS-E973 - 0.556559																																							
		puromycin - 0.6042523	NMS-E973 - 0.6042523																																							
		MG-262 - 0.6513953	NMS-E973 - 0.6513953																																							
			NMS-SN38 - 0.7871002																																							
			PHA-793887 - 0.767364																																							
		withaferin A - 0.6663354	NMS-E973 - 0.6663354																																							
			NMS-SN38 - 0.7681578																																							
		trifluoperazine - 0.6738632	NMS-E973 - 0.6738632																																							
		NMS-Doxorubicin - 0.6950551	NMS-E973 - 0.6950551																																							
			NMS-SN38 - 0.2860369																																							
			PHA-793887 - 0.4421239																																							
		lomustine - 0.7082947	NMS-E973 - 0.7082947																																							
			NMS-SN38 - 0.7692162																																							
		disulfiram - 0.7109033	NMS-E973 - 0.7109033																																							
		HC toxin - 0.7228326	NMS-E973 - 0.7228326																																							
			NMS-SN38 - 0.7464498																																							

This button generates a dialog with the analysis of common genes between selected nodes.

In particular, you will have two **On/Off** tables:

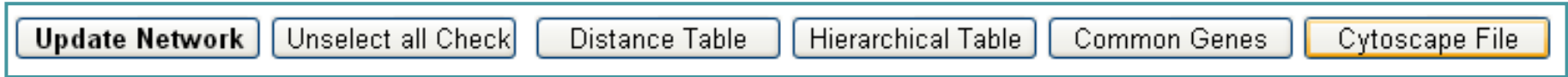
1. Down Regulated genes
2. Up Regulated genes

Down Regulated common genes - On/Off Table

Gene	PHA-793887	NMS-E973	NMS-SN38
ARMC8 - 219094_at	X	0	X
ATAD2B - 213387_at	X	0	X
BUB1B - 203755_at	X	0	X
C9orf91 - 221865_at	X	X	0
CCNE2 - 211814_s_at	X	X	0
CEBPB - 212501_at	X	X	0
CENPA - 204962_s_at	X	0	X
CENPE - 205046_at	X	0	X
CHAC1 - 219270_at	X	X	0
EML1 - 204796_at	X	0	X
ID4 - 209291_at	X	X	0
INHBE - 210587_at	X	X	X
JMJD4 - 218560_s_at	X	X	0
KIF11 - 204444_at	X	0	X
KIF18A - 221258_s_at	X	0	X
MEIS1 - 204069_at	X	0	X
METTL1 - 204027_s_at	X	X	0
NDC80 - 204162_at	X	0	X
PAFAH1B1 - 211547_s_at	X	0	X
PDS5B - 204742_s_at	X	0	X
PLK1 - 202240_at	X	0	X
PRIM1 - 205053_at	X	X	0
PSRC1 - 201896_s_at	X	0	X
RASAL2 - 219026_s_at	X	0	X
RBL1 - 205296_at	X	0	X
SAP30 - 204900_x_at	X	0	X
SR140 - 212061_at	X	0	X
SRSF3 - 208673_s_at	X	0	X
TBC1D30 - 213913_s_at	X	0	X
TRIB1 - 202241_at	X	X	0
TRMT61B - 221229_s_at	X	X	X
TSEN2 - 219581_at	X	X	0
VAV3 - 218807_at	X	0	X
VLDLR - 209822_s_at	X	0	X
CYP24A1 - 206504_at	0	X	X
GMPS - 214431_at	0	X	X
MAP3K5 - 203837_at	0	X	X
MSH2 - 209421_at	0	X	X
TP63 - 209863_s_at	0	X	X



Cytoscape is an open source bioinformatics software for visualization and analysis of interactions networks.

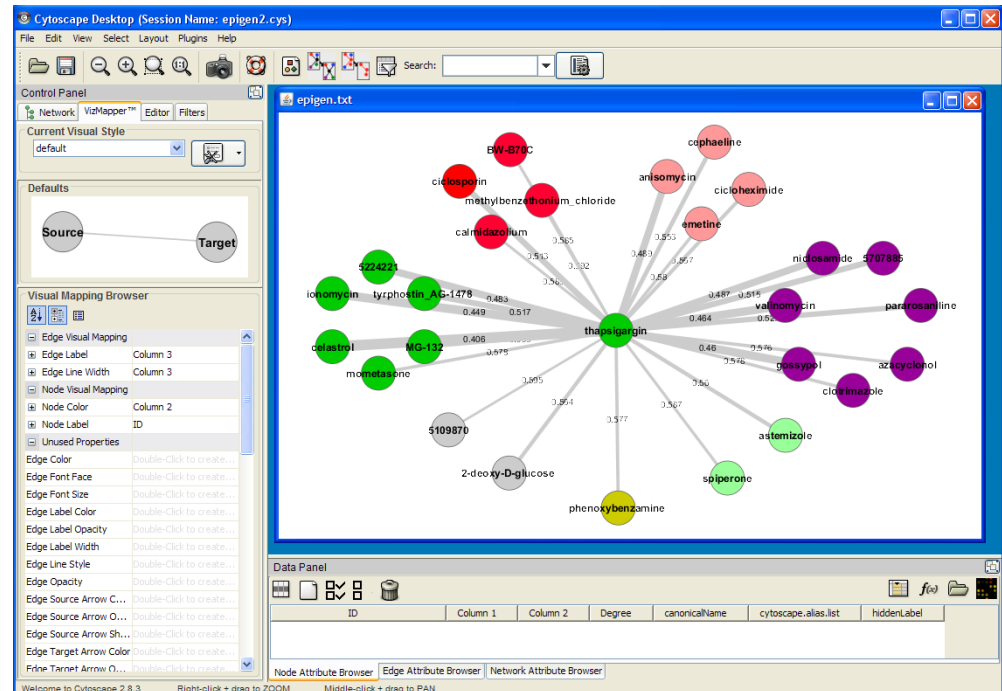


Creates a **SIF** (Simple Interaction Format) file: a text format invented for Cytoscape. It consists of 3 columns: source, interaction type (distance), and target.

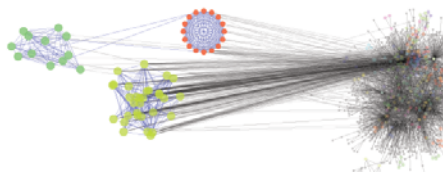
```
nodeA <relationship type> nodeB
nodeC <relationship type> nodeA
nodeD <relationship type> nodeE
```



In Cytoscape:
File → *Import* → *Network*
(Multiple File Types)



Cytoscape



<http://www.cytoscape.org/>




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The Search tab provides three different search mode: "Search for synonyms", "Search for text in the nodes description", "Search for nodes by distance starting one node".



 **Mantra 2.0** Mode of Action by NeTwork Analysis

Home page About Network **Search** Analysis

Node Search Page

Search for synonyms:


Search for text in the nodes description:

Search for nodes by distance:
Node:

Find Nodes:

Selected Nodes:

Selecting one node from the search results, it is possible to display the node description and experiments detail.


Mantra 2.0 Mode of Action by NeTwork Analysis

Home page
About
Network
Search
Analysis

Node Search Page

Search for synonyms:

Search for text in the nodes description:
 ←

Search for nodes by distance:
 Node:

Find Nodes:

Selected Nodes:

List of experiments

name	data_ins	chip_name	category	description	timing	dosage	perturbation	cell_line
Doxorubicin	23/01/2013 14:59:23	HG-U133_Plus_2	Other	Nerviano Medical Sciences (NMS) - MCF7 treated Doxorubicin	unknown	unknown	unknown	MCF7

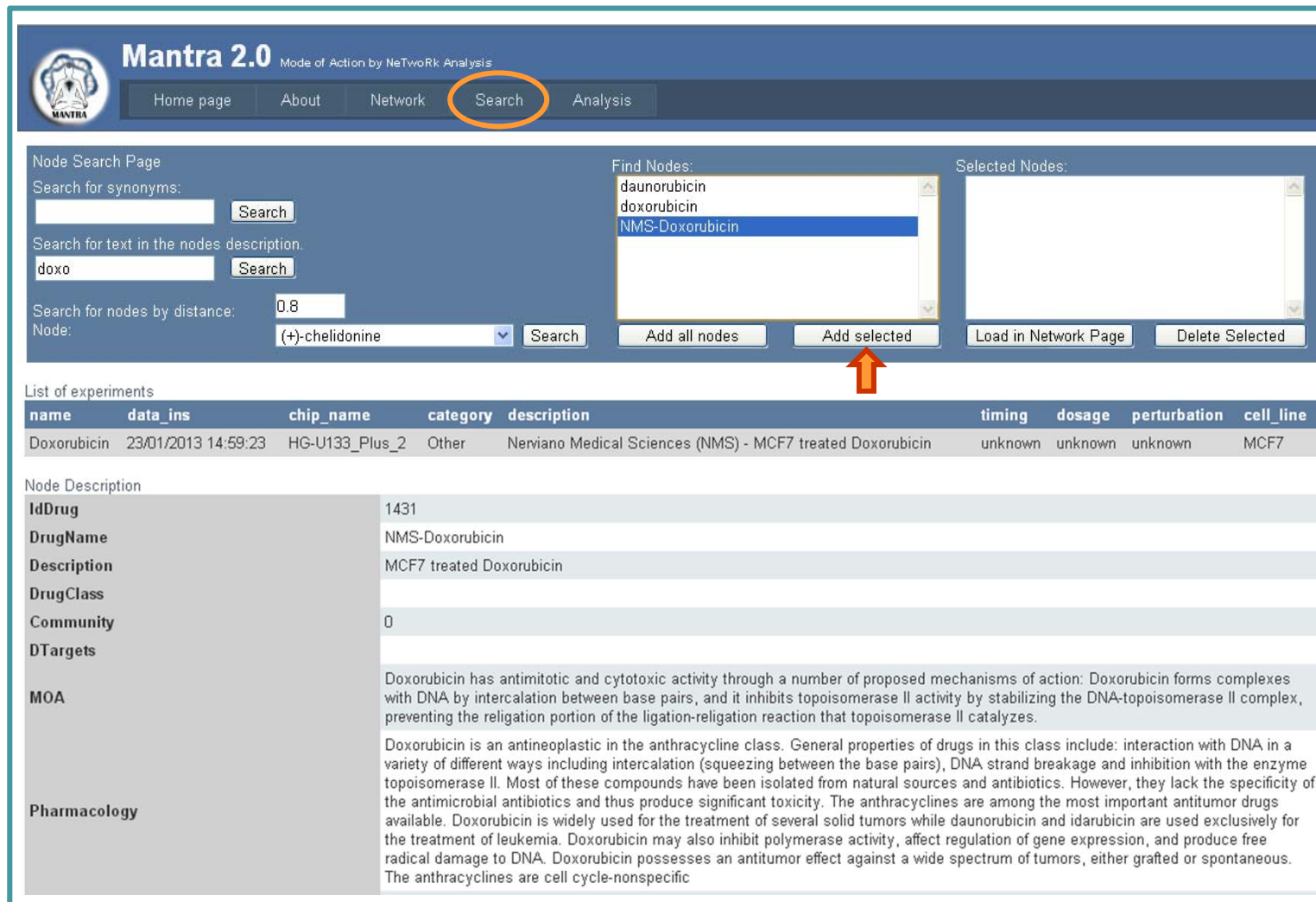
Node Description

IdDrug	1431
DrugName	NMS-Doxorubicin
Description	MCF7 treated Doxorubicin
DrugClass	
Community	0
DTargets	
MOA	Doxorubicin has antimitotic and cytotoxic activity through a number of proposed mechanisms of action: Doxorubicin forms complexes with DNA by intercalation between base pairs, and it inhibits topoisomerase II activity by stabilizing the DNA-topoisomerase II complex, preventing the religation portion of the ligation-religation reaction that topoisomerase II catalyzes.
Pharmacology	Doxorubicin is an antineoplastic in the anthracycline class. General properties of drugs in this class include: interaction with DNA in a variety of different ways including intercalation (squeezing between the base pairs), DNA strand breakage and inhibition with the enzyme topoisomerase II. Most of these compounds have been isolated from natural sources and antibiotics. However, they lack the specificity of the antimicrobial antibiotics and thus produce significant toxicity. The anthracyclines are among the most important antitumor drugs available. Doxorubicin is widely used for the treatment of several solid tumors while daunorubicin and idarubicin are used exclusively for the treatment of leukemia. Doxorubicin may also inhibit polymerase activity, affect regulation of gene expression, and produce free radical damage to DNA. Doxorubicin possesses an antitumor effect against a wide spectrum of tumors, either grafted or spontaneous. The anthracyclines are cell cycle-nonspecific

Node info

Experiments info

The search results can be added, all or individually, at the "Selected Nodes" box.



Mantra 2.0 Mode of Action by NeTwork Analysis

Home page About Network **Search** Analysis

Node Search Page

Search for synonyms: Search

Search for text in the nodes description: Search

Search for nodes by distance: Node: Search

Find Nodes:

- daunorubicin
- doxorubicin
- NMS-Doxorubicin**

Selected Nodes:

Add all nodes Add selected Load in Network Page Delete Selected

List of experiments

name	data_ins	chip_name	category	description	timing	dosage	perturbation	cell_line
Doxorubicin	23/01/2013 14:59:23	HG-U133_Plus_2	Other	Nerviano Medical Sciences (NMS) - MCF7 treated Doxorubicin	unknown	unknown	unknown	MCF7

Node Description

IdDrug 1431

DrugName NMS-Doxorubicin

Description MCF7 treated Doxorubicin

DrugClass


Community 0

DTargets

MOA Doxorubicin has antimitotic and cytotoxic activity through a number of proposed mechanisms of action: Doxorubicin forms complexes with DNA by intercalation between base pairs, and it inhibits topoisomerase II activity by stabilizing the DNA-topoisomerase II complex, preventing the religation portion of the ligation-religation reaction that topoisomerase II catalyzes.

Pharmacology Doxorubicin is an antineoplastic in the anthracycline class. General properties of drugs in this class include: interaction with DNA in a variety of different ways including intercalation (squeezing between the base pairs), DNA strand breakage and inhibition with the enzyme topoisomerase II. Most of these compounds have been isolated from natural sources and antibiotics. However, they lack the specificity of the antimicrobial antibiotics and thus produce significant toxicity. The anthracyclines are among the most important antitumor drugs available. Doxorubicin is widely used for the treatment of several solid tumors while daunorubicin and idarubicin are used exclusively for the treatment of leukemia. Doxorubicin may also inhibit polymerase activity, affect regulation of gene expression, and produce free radical damage to DNA. Doxorubicin possesses an antitumor effect against a wide spectrum of tumors, either grafted or spontaneous. The anthracyclines are cell cycle-nonspecific

The selected nodes can be loaded directly in Network Page clicking on “Load in Network Page” button.


Mantra 2.0 Mode of Action by NeTwoRk Analysis

Home page
About
Network
Search
Analysis

Node Search Page

Search for synonyms:

Search for text in the nodes description:

Search for nodes by distance:


Node:

Find Nodes:

daunorubicin
 doxorubicin
 NMS-Doxorubicin

Selected Nodes:

doxorubicin
 NMS-Doxorubicin



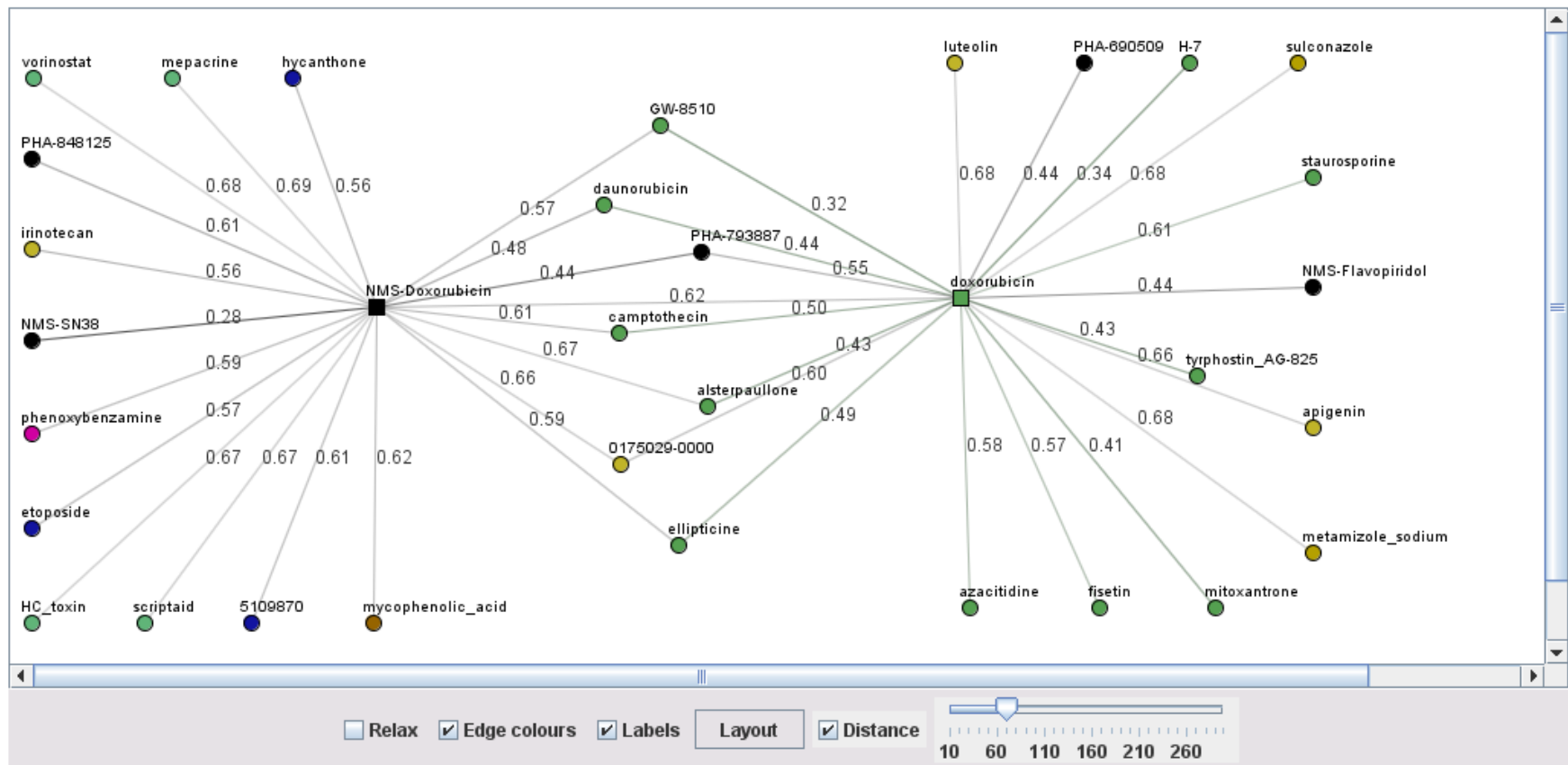
List of experiments

name	data_ins	chip_name	category	description	timing	dosage	perturbation	cell_line
Doxorubicin	23/01/2013 14:59:23	HG-U133_Plus_2	Other	Nerviano Medical Sciences (NMS) - MCF7 treated Doxorubicin	unknown	unknown	unknown	MCF7

Node Description

IdDrug	1431
DrugName	NMS-Doxorubicin
Description	MCF7 treated Doxorubicin
DrugClass	
Community	0
DTargets	
MOA	Doxorubicin has antimitotic and cytotoxic activity through a number of proposed mechanisms of action: Doxorubicin forms complexes with DNA by intercalation between base pairs, and it inhibits topoisomerase II activity by stabilizing the DNA-topoisomerase II complex, preventing the religation portion of the ligation-religation reaction that topoisomerase II catalyzes.
Pharmacology	Doxorubicin is an antineoplastic in the anthracycline class. General properties of drugs in this class include: interaction with DNA in a variety of different ways including intercalation (squeezing between the base pairs), DNA strand breakage and inhibition with the enzyme topoisomerase II. Most of these compounds have been isolated from natural sources and antibiotics. However, they lack the specificity of the antimicrobial antibiotics and thus produce significant toxicity. The anthracyclines are among the most important antitumor drugs available. Doxorubicin is widely used for the treatment of several solid tumors while daunorubicin and idarubicin are used exclusively for the treatment of leukemia. Doxorubicin may also inhibit polymerase activity, affect regulation of gene expression, and produce free radical damage to DNA. Doxorubicin possesses an antitumor effect against a wide spectrum of tumors, either grafted or spontaneous. The anthracyclines are cell cycle-nonspecific

The search results can be selected and loaded directly in Network Page.





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Input

Step 1: Uploads the Experiments

Upload ProbeSetIDs List

Analysis Name:

Chip Name:

Upload file: Nessun file selezionato

Step 2: Create New Nodes

New node

All Select Experiment Category

Select an experiment Select all experiments

User experiments list

Selected	id_exp	name	data_ins	chip_name	category	description
<input type="checkbox"/>	36	CDK-125	22/01/2013 12:06:51	HG-U133_Plus_2	Other	Nerviano Medical Sciences (NMS)-A2780 treated CDK-125
<input type="checkbox"/>	38	CDK-125	23/01/2013 09:59:03	HG-U133_Plus_2	Other	Nerviano Medical Sciences (NMS)-MCF7 treated CDK-125
<input checked="" type="checkbox"/>	40	Tanespimycin-17AAG	23/01/2013 11:22:22	HG-U133_Plus_2	Other	Nerviano Medical Sciences (NMS)-MCF7 treated Tanespimycin-17AAG

Node name:

Node description:

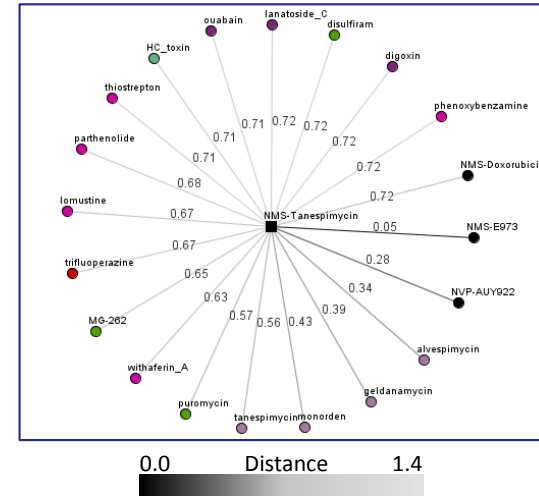
Node Category:

Is Private



Output

Network View



Tabulated Results

Selected Drug	Distance	Drug2	Community	TherapeuticIndications
NMS-Tanespimycin	0.391792	geldanamycin	28	Gram-Negative Bacterial InfectionsProtozoan In Gram-Positive Bacterial InfectionsMycoses Ne
NMS-Tanespimycin	0.431153	monorden	28	
NMS-Tanespimycin	0.673294	trifluoperazine	100	Vomiting
NMS-Tanespimycin	0.675602	lomustine	104	
NMS-Tanespimycin	0.685952	parthenolide	104	Neoplasms Bacterial Infections

In step 1, the user uploads the experiments data in affymetrix-compatible format. **In step 2**, the user can filter the experiments based on the characteristics and annotation, and create new nodes. After processing, the recalculated network is available in a viewer of web-based interactive and in several tabulated formats (as a Distance Table, a Cytoscape-compatible format, and browser tables with links to external source databases).



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- The potential of the massive quantity of public available gene expression data has not been fully exploited.
- A significant number of published works showed that it is possible to identify drug repositioning opportunities by using genome-wide signature-matching methods.
- MANTRA web tool is the construction of unique platform in which it is possible to explore and expand the network of drugs. In addition to hypothesize new therapeutic applications for approved drugs, already present in the network, it is possible to study the repositioning of new drugs by analyzing their neighbors.

Thanks !

