

GS01 0163

Analysis of Microarray Data

Keith Baggerly and Kevin Coombes
Section of Bioinformatics
Department of Biostatistics and Applied Mathematics
UT M. D. Anderson Cancer Center
kabagg@mdanderson.org
kcoombes@mdanderson.org

21 October 2004

Lecture 15: Regulatory networks

- PathArt
- Ingenuity

PathArt

Jubilant Biosys – PathArt – Netscape

File Edit View Go Bookmarks Tools Window Help

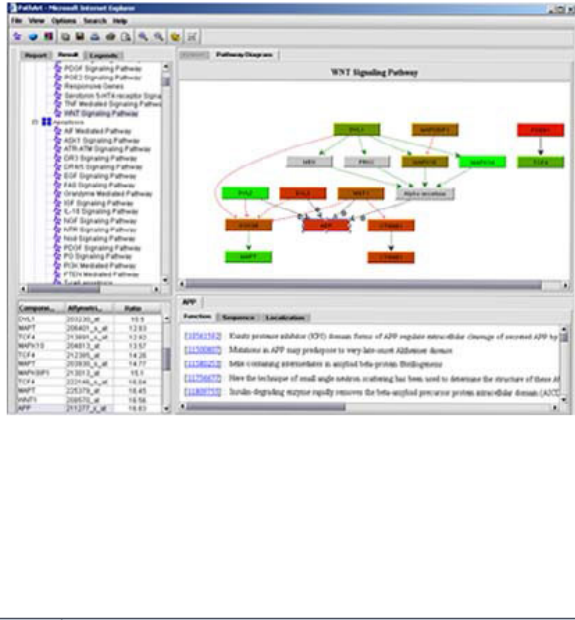
http://insidebioinfo.mdacc.tmc.edu:8080/pathart/index.html

Home Radio Bookmarks Google Bioinformatics ...

JUBILANT BIOSYS

PathArt™

PathArt™ is a curated database of biomolecular interactions with tools for searching, analysis and visualization of data for use by microarray researchers and identification of potential drug targets. Pathway diagrams in PathArt™ are dynamically generated from data in the database. PathArt™ is accessible via any Java enabled browser and provides enterprise wide access to data stored in an Oracle database.

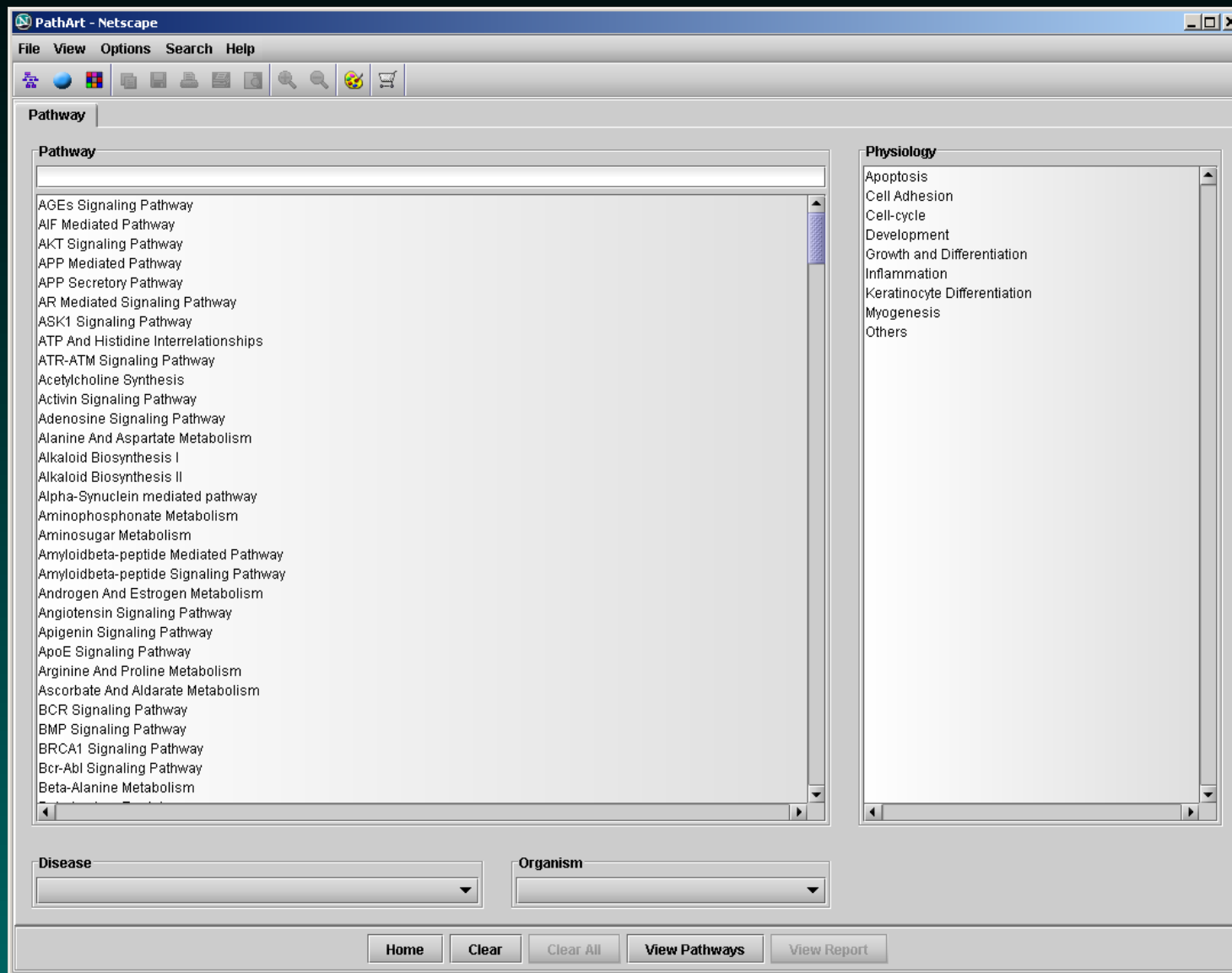


The screenshot shows the PathArt web application interface. On the left, there is a list of pathways under the heading 'Pathway Diagrams'. The list includes various signaling pathways such as WNT Signaling Pathway, TGF-beta Signaling Pathway, and others. On the right, a detailed diagram of the WNT Signaling Pathway is displayed, showing the flow of signaling molecules and their interactions. The diagram includes components like Wnt, Receptor, GPCR, and various proteins involved in the pathway.

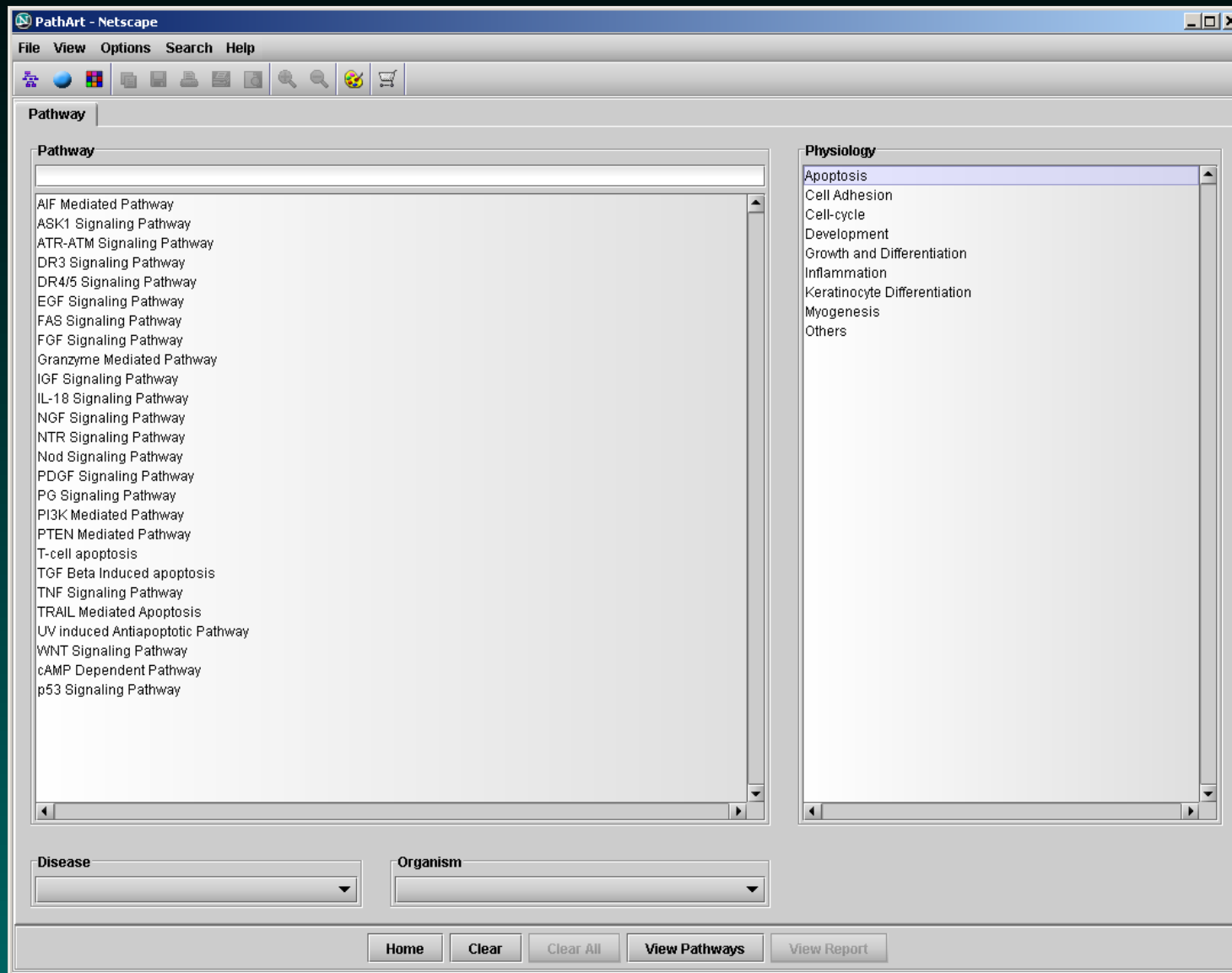
Features

- Coverage of about 900 regulatory and signaling pathways across species.
- Browse pathways by organism, disease and other classifications.
- Coverage of protein-protein interaction.
- Information on knockout and mutagenesis studies.
- Search for pathways by specific genes.
- Coverage of 17 high priority diseases and disease responsive genes.
- Generate customized reports on genes and interactions of interest.
- Allows use of microarray expression data to search relevant pathways based on expression level. Allows use of Agilent and Affymetrix data.
- Comprehensive information on all participating biomolecules, curated from scientific journals and databases.

PathArt opening screen



PathArt as pathway browser



PTEN mediated pathway

PathArt - Netscape

File View Options Search Help

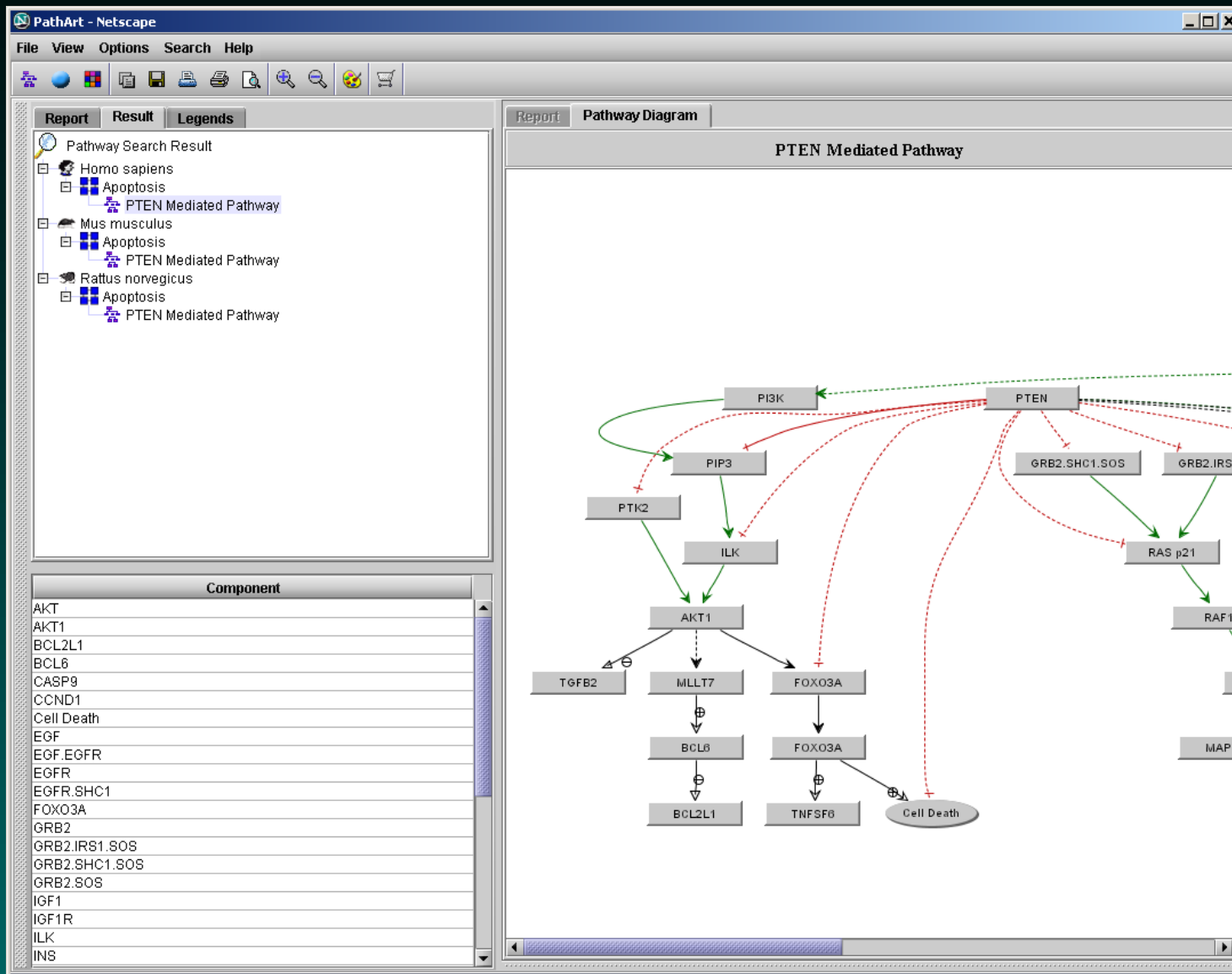
Report Result

Pathway Search Result

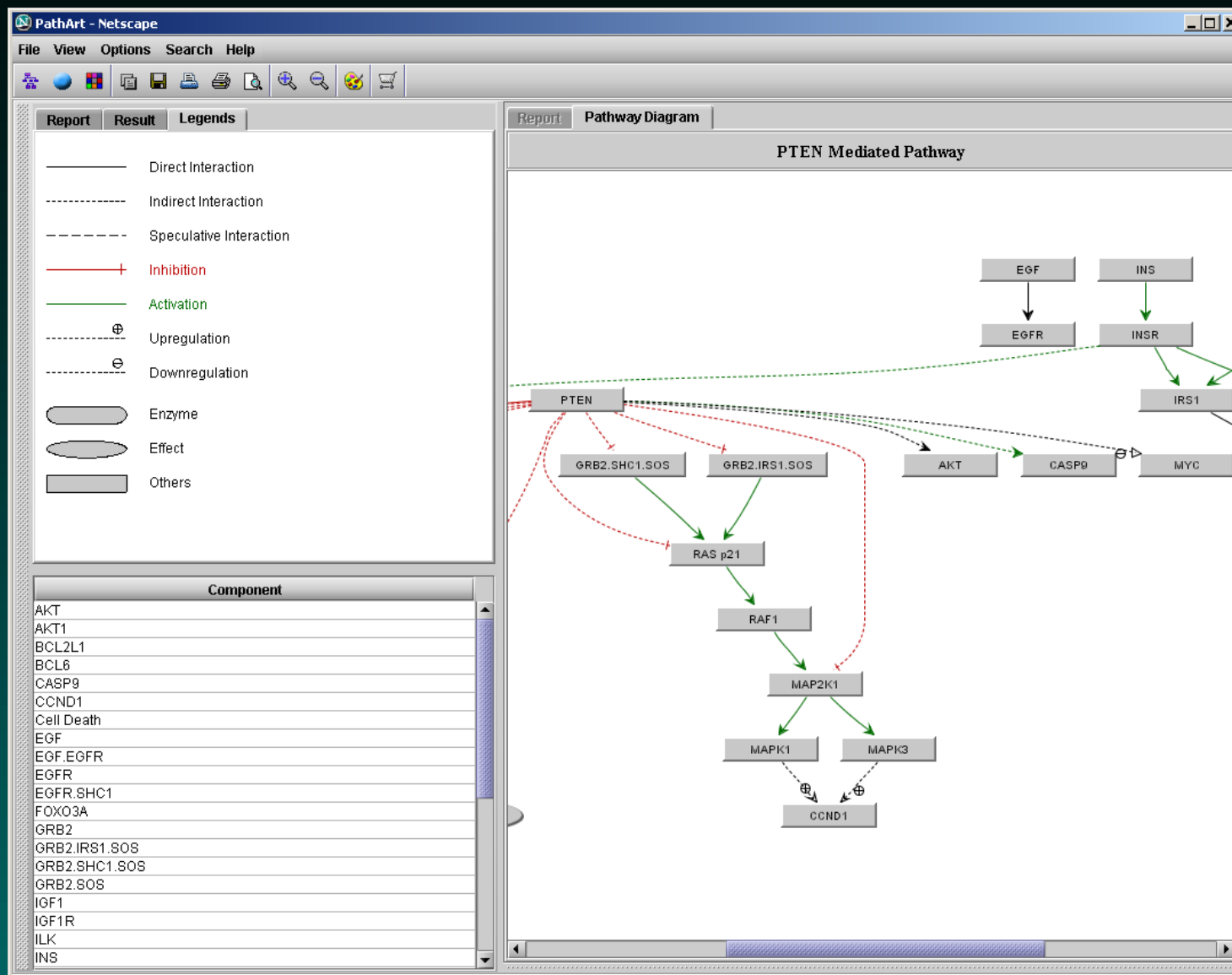
- Homo sapiens
 - Apoptosis
 - PTEN Mediated Pathway
- Mus musculus
 - Apoptosis
 - PTEN Mediated Pathway
- Rattus norvegicus
 - Apoptosis
 - PTEN Mediated Pathway

Organism	Physiology/Disease	Pathway	Gene Name	Gene Id
Homo sapiens			<input type="checkbox"/> AKT	<input type="checkbox"/>
			<input type="checkbox"/> AKT1	<input type="checkbox"/>
			<input type="checkbox"/> BCL2L1	<input type="checkbox"/>
			<input type="checkbox"/> BCL6	<input type="checkbox"/>
			<input type="checkbox"/> CASP9	<input type="checkbox"/>
			<input type="checkbox"/> CCND1	<input type="checkbox"/>
			<input type="checkbox"/> EGF	<input type="checkbox"/>
			<input type="checkbox"/> EGFR	<input type="checkbox"/>
			<input type="checkbox"/> FOXO3A	<input type="checkbox"/>
			<input type="checkbox"/> GRB2	<input type="checkbox"/>
			<input type="checkbox"/> IGF1	<input type="checkbox"/>
			<input type="checkbox"/> IGF1R	<input type="checkbox"/>
			<input type="checkbox"/> ILK	<input type="checkbox"/>
			<input type="checkbox"/> INS	<input type="checkbox"/>
			<input type="checkbox"/> INSR	<input type="checkbox"/>
			<input type="checkbox"/> IRS1	<input type="checkbox"/>
			<input type="checkbox"/> MAP2K1	<input type="checkbox"/>
			<input type="checkbox"/> MAPK1	<input type="checkbox"/>
			<input type="checkbox"/> MAPK3	<input type="checkbox"/>
			<input type="checkbox"/> MLLT7	<input type="checkbox"/>
			<input type="checkbox"/> MYC	<input type="checkbox"/>
			<input type="checkbox"/> PI3K	<input type="checkbox"/>
			<input type="checkbox"/> PIP3	<input type="checkbox"/>
			<input type="checkbox"/> PTEN	<input type="checkbox"/>
			<input type="checkbox"/> PTK2	<input type="checkbox"/>
			<input type="checkbox"/> RAF1	<input type="checkbox"/>
			<input type="checkbox"/> RAS p21	<input type="checkbox"/>
			<input type="checkbox"/> SHC1	<input type="checkbox"/>
			<input type="checkbox"/> SOS	<input type="checkbox"/>
			<input type="checkbox"/> TGFB2	<input type="checkbox"/>
			<input type="checkbox"/> TNFSF6	<input type="checkbox"/>
			<input type="checkbox"/> Akt1	<input type="checkbox"/>
			<input type="checkbox"/> Bcl2	<input type="checkbox"/>
			<input type="checkbox"/> Car3	<input type="checkbox"/>

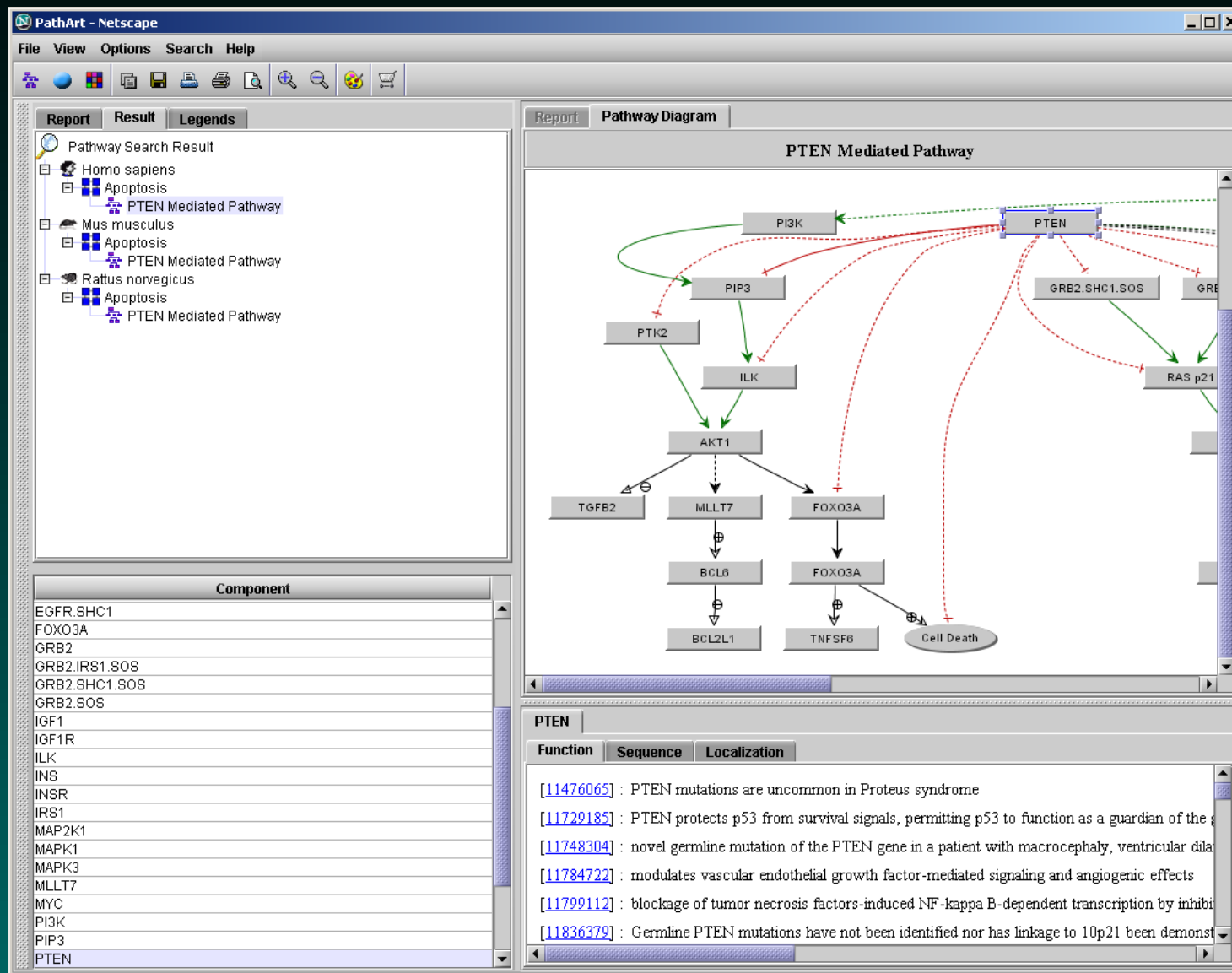
PTEN pathway diagram



PathArt symbol legend



Evidence supports inclusion of genes in diagrams



Links go live to NCBI

Entrez PubMed - Netscape

File Edit View Go Bookmarks Tools Window Help

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11729185&dopt=Abstract

Search

Home Radio Bookmarks Google Bioinformatics ...

NCBI PubMed National Library of Medicine NLM

Entrez PubMed Nucleotide Protein Genome Structure OMIM PMC Journals Books

Search PubMed for Go Clear

Limits Preview/Index History Clipboard Details

Display Abstract Show: 20 Sort Send to Text

About Entrez

Text Version

Entrez PubMed

Overview

Help | FAQ

Tutorial

New/Noteworthy

E-Utilities

PubMed Services

Journals Database

MeSH Database

Single Citation

Matcher

Batch Citation Matcher

Clinical Queries

LinkOut

Cubby

Related Resources

Order Documents

NLM Catalog

NLM Gateway

TOXNET

Consumer Health

Clinical Alerts

ClinicalTrials.gov

PubMed Central

1: J Biol Chem. 2002 Feb 15;277(7):5484-9. Epub 2001 Nov 29. [Related Articles, Links](#)

[FREE full text article at www.jbc.org](#)

PTEN protects p53 from Mdm2 and sensitizes cancer cells to chemotherapy.

Mayo LD, Dixon JE, Durden DL, Tonks NK, Donner DB.

Department of Microbiology, Indiana University School of Medicine, Indianapolis, Indiana 46202, USA.

The PTEN tumor suppressor protein inhibits phosphatidylinositol 3-kinase (PI3K)/Akt signaling that promotes translocation of Mdm2 into the nucleus. When restricted to the cytoplasm, Mdm2 is degraded. The ability of PTEN to inhibit the nuclear entry of Mdm2 increases the cellular content and transactivation of the p53 tumor suppressor protein. Retroviral transduction of PTEN into U87MG (PTEN null) glioblastoma cells increases p53 activity and expression of p53 target genes and induces cell cycle arrest. U87MG/PTEN glioblastoma cells are more sensitive than U87MG/PTEN null cells to death induced by etoposide, a chemotherapeutic agent that induces DNA damage. Previously, tumor suppressor proteins have been supposed to act individually to suppress cancers. Our results establish a direct connection between the activities of two major tumor suppressors and show that they act together to respond to stresses and malignancies. PTEN protects p53 from survival signals, permitting p53 to function as a guardian of the genome. By virtue of its capacity to protect p53, PTEN can sensitize tumor cells to chemotherapy that relies on p53 activity. p53 induces PTEN gene expression, and here it is shown that PTEN protects p53, indicating that a positive feedback loop may amplify the cellular response to stress, damage, and cancer.

PMID: 11729185 [PubMed - indexed for MEDLINE]

Display Abstract Show: 20 Sort Send to Text

[Write to the Help Desk](#)

[NCBI](#) | [NLM](#) | [NIH](#)

[Department of Health & Human Services](#)

[Privacy Statement](#) | [Freedom of Information Act](#) | [Disclaimer](#)

Oct 13 2004 09:44:09

PathArt Menu to load microarray data

The screenshot displays the PathArt software interface within a Netscape browser window. The interface includes a menu bar (File, View, Options, Search, Help) and a toolbar. The 'Import' menu is open, showing 'Microarray' as the selected option. The 'Print Preview' section shows a search result for 'PTEN Mediated Pathway' across different species (Homo sapiens, Mus musculus, Rattus norvegicus). The main window displays the 'PTEN Mediated Pathway' diagram, which illustrates the signaling pathway involving PTEN, PI3K, PIP3, PTK2, ILK, AKT1, TGFβ2, MLLT7, BCL6, BCL2L1, FOXO3A, TNFSF8, and RAS p21. The diagram shows various interactions, including activation (solid green arrows), inhibition (dashed red arrows), and feedback loops. A 'Component' list is visible on the left, containing genes like EGFR, SHC1, FOXO3A, GRB2, and PTEN. The bottom panel shows the 'PTEN' entry, with tabs for 'Function', 'Sequence', and 'Localization'. The 'Function' tab is active, displaying a list of PubMed references related to PTEN mutations and their effects on signaling pathways.

PTEN Mediated Pathway

Component

- EGFR.SHC1
- FOXO3A
- GRB2
- GRB2.IRS1.SOS
- GRB2.SHC1.SOS
- GRB2.SOS
- IGF1
- IGF1R
- ILK
- INS
- INSR
- IRS1
- MAP2K1
- MAPK1
- MAPK3
- MLLT7
- MYC
- PI3K
- PIP3
- PTEN

PTEN

Function **Sequence** **Localization**

- [11476065] : PTEN mutations are uncommon in Proteus syndrome
- [11729185] : PTEN protects p53 from survival signals, permitting p53 to function as a guardian of the genome
- [11748304] : novel germline mutation of the PTEN gene in a patient with macrocephaly, ventricular dilatation
- [11784722] : modulates vascular endothelial growth factor-mediated signaling and angiogenic effects
- [11799112] : blockage of tumor necrosis factors-induced NF-kappa B-dependent transcription by inhibition of I-kappa B kinase
- [11836379] : Germline PTEN mutations have not been identified nor has linkage to 10p21 been demonstrated

PathArt with array info loaded

PathArt - Netscape

File View Options Search Help

Microarray Pathway

Normalizer Cluster

Microarray Data

Id Type: Unigenel ☒ Show unselected genes

ID	Expression ...
Hs.250616	-4.620291
Hs.75309	7.709446
Hs.440382	5.294954
Hs.440382	6.264828
Hs.24332	-6.522626
Hs.367688	-7.401072
Hs.272927	-8.724433
Hs.272927	-9.049278
Hs.102471	-7.19262
Hs.13604	5.809353
Hs.143251	-5.02975
Hs.48348	-5.997128
Hs.439031	-5.367195
Hs.129159	5.053361
Hs.74562	4.872108
Hs.447905	5.658341
Hs.82568	-5.931616
Hs.184298	4.320148
Hs.194662	-4.741693
Hs.8364	-6.815697
Hs.133321	-7.056189
Hs.58561	-6.367254
Hs.121576	6.288705
Hs.35380	-6.576627
Hs.449894	5.167162
Hs.42173	6.808548
Hs.102607	-5.105139
Hs.110028	-6.922639
Hs.212787	-6.415029
Hs.435733	-5.73705
Hs.136295	-7.008182
Hs.21107	-5.322678
Hs.151411	-5.303271
Hs.181046	-4.771713
Hs.342874	-8.413357
Hs.114062	-5.886276
Hs.257111	6.435214
Hs.377972	-6.076756
Hs.459470	6.3389

Normalization Method

☒ Global

☐ Local Degree of Polynomial 1 Smoothing Parameter 0.33

Plot

Scatter Plot

Log Ratio

Min Max

Apply

Home Clear Clear All View Pathways View Report

Microarray-selected pathways

PathArt - Netscape

File View Options Search Help

Report Result

Microarray Search Result

- Homo sapiens
 - Acquired Immuno Deficiency Syndrome
 - CCR5-mediated Pathway
 - CD28 Mediated Pathway
 - CD4-dependent Pathway
 - CD40L Signaling Pathway
 - CXCR4-mediated Pathway
 - Env Signaling Pathway
 - LPS Signaling Pathway
 - Nef-mediated Pathway
 - Responsive Genes
 - TNFalpha Signaling Pathway
 - Tat Signaling Pathway
 - Vpr Signaling Pathway
 - Alzheimers
 - Amyloidbeta-peptide Mediated Pathway
 - IGF1 Signaling Pathway
 - Notch Signaling Pathway
 - Responsive Genes
 - Serotonin 5-HT4 receptor Signaling Pathway
 - TNF Mediated Signaling Pathway
 - WNT Signaling Pathway
 - Apoptosis
 - Alf Mediated Pathway
 - ASK1 Signaling Pathway
 - ATR-ATM Signaling Pathway
 - DR3 Signaling Pathway
 - DR4/5 Signaling Pathway
 - EGF Signaling Pathway
 - FAS Signaling Pathway
 - Granzyme Mediated Pathway
 - IGF Signaling Pathway
 - IL-18 Signaling Pathway
 - Nod Signaling Pathway
 - PTEN Mediated Pathway
 - TGF Beta Induced apoptosis
 - TNF Signaling Pathway
 - TRAIL Mediated Apoptosis
 - WNT Signaling Pathway
 - p53 Signaling Pathway
 - Asthma
 - Bradykinin Signaling Pathway
 - Cytokines Signaling Pathway
 - EGF Signaling Pathway

Organism	Physiology/Disease	Pathway	Gene Name	Gene Id
		<input type="checkbox"/> CCR5-mediated Pat...	<input type="checkbox"/> CXCL12	<input type="checkbox"/> Hs.436042
			<input type="checkbox"/> TNF	<input type="checkbox"/> Hs.241570
		<input type="checkbox"/> CD28 Mediated Path...	<input type="checkbox"/> CDK9	<input type="checkbox"/> Hs.150423
			<input type="checkbox"/> CXCL12	<input type="checkbox"/> Hs.436042
		<input type="checkbox"/> CD4-dependent Path...	<input type="checkbox"/> TNF	<input type="checkbox"/> Hs.241570
			<input type="checkbox"/> TNF	<input type="checkbox"/> Hs.241570
		<input type="checkbox"/> CD40L Signaling Pat...	<input type="checkbox"/> TNFRSF5	<input type="checkbox"/> Hs.504816
			<input type="checkbox"/> CXCL12	<input type="checkbox"/> Hs.436042
		<input type="checkbox"/> CXCR4-mediated Pa...	<input type="checkbox"/> TNF	<input type="checkbox"/> Hs.241570
			<input type="checkbox"/> MYC	<input type="checkbox"/> Hs.202453
		<input type="checkbox"/> Env Signaling Pathw...	<input type="checkbox"/> PRKCA	<input type="checkbox"/> Hs.349611
			<input type="checkbox"/> STAT3	<input type="checkbox"/> Hs.421342
	<input type="checkbox"/> Acquired Immuno Defici...	<input type="checkbox"/> LPS Signaling Path...	<input type="checkbox"/> IRAK1	<input type="checkbox"/> Hs.182018
			<input type="checkbox"/> TNF	<input type="checkbox"/> Hs.241570
		<input type="checkbox"/> Nef-mediated Pathw...	<input type="checkbox"/> STAT3	<input type="checkbox"/> Hs.421342
			<input type="checkbox"/> TNF	<input type="checkbox"/> Hs.241570
		<input type="checkbox"/> Responsive Genes	<input type="checkbox"/> MYC	<input type="checkbox"/> Hs.202453
		<input type="checkbox"/> TNFalpha Signaling ...	<input type="checkbox"/> NCOA1	<input type="checkbox"/> Hs.386092
			<input type="checkbox"/> TNF	<input type="checkbox"/> Hs.241570
		<input type="checkbox"/> Tat Signaling Pathway	<input type="checkbox"/> ITGB1	<input type="checkbox"/> Hs.287797
			<input type="checkbox"/> MAPK9	<input type="checkbox"/> Hs.348446
			<input type="checkbox"/> TNF	<input type="checkbox"/> Hs.241570
			<input type="checkbox"/> TRAF4	<input type="checkbox"/> Hs.8375
		<input type="checkbox"/> Vpr Signaling Pathw...	<input type="checkbox"/> CDC2	<input type="checkbox"/> Hs.334562
			<input type="checkbox"/> HRB2	<input type="checkbox"/> Hs.269857
			<input type="checkbox"/> TNF	<input type="checkbox"/> Hs.241570
		<input type="checkbox"/> Amyloidbeta-peptide...	<input type="checkbox"/> CDK5	<input type="checkbox"/> Hs.166071
			<input type="checkbox"/> IGF1	<input type="checkbox"/> Hs.308053
			<input type="checkbox"/> TNF	<input type="checkbox"/> Hs.241570
	<input type="checkbox"/> Alzheimers	<input type="checkbox"/> IGF1 Signaling Path...	<input type="checkbox"/> IGF1	<input type="checkbox"/> Hs.308053
		<input type="checkbox"/> Notch Signaling Pat...	<input type="checkbox"/> RBPSUH	<input type="checkbox"/> Hs.347340
			<input type="checkbox"/> CRYAB	<input type="checkbox"/> Hs.408767
		<input type="checkbox"/> Responsive Genes	<input type="checkbox"/> HSPB1	<input type="checkbox"/> Hs.76067
			<input type="checkbox"/> SERPINA3	<input type="checkbox"/> Hs.76353

Pathways are organized by disease

PathArt - Netscape

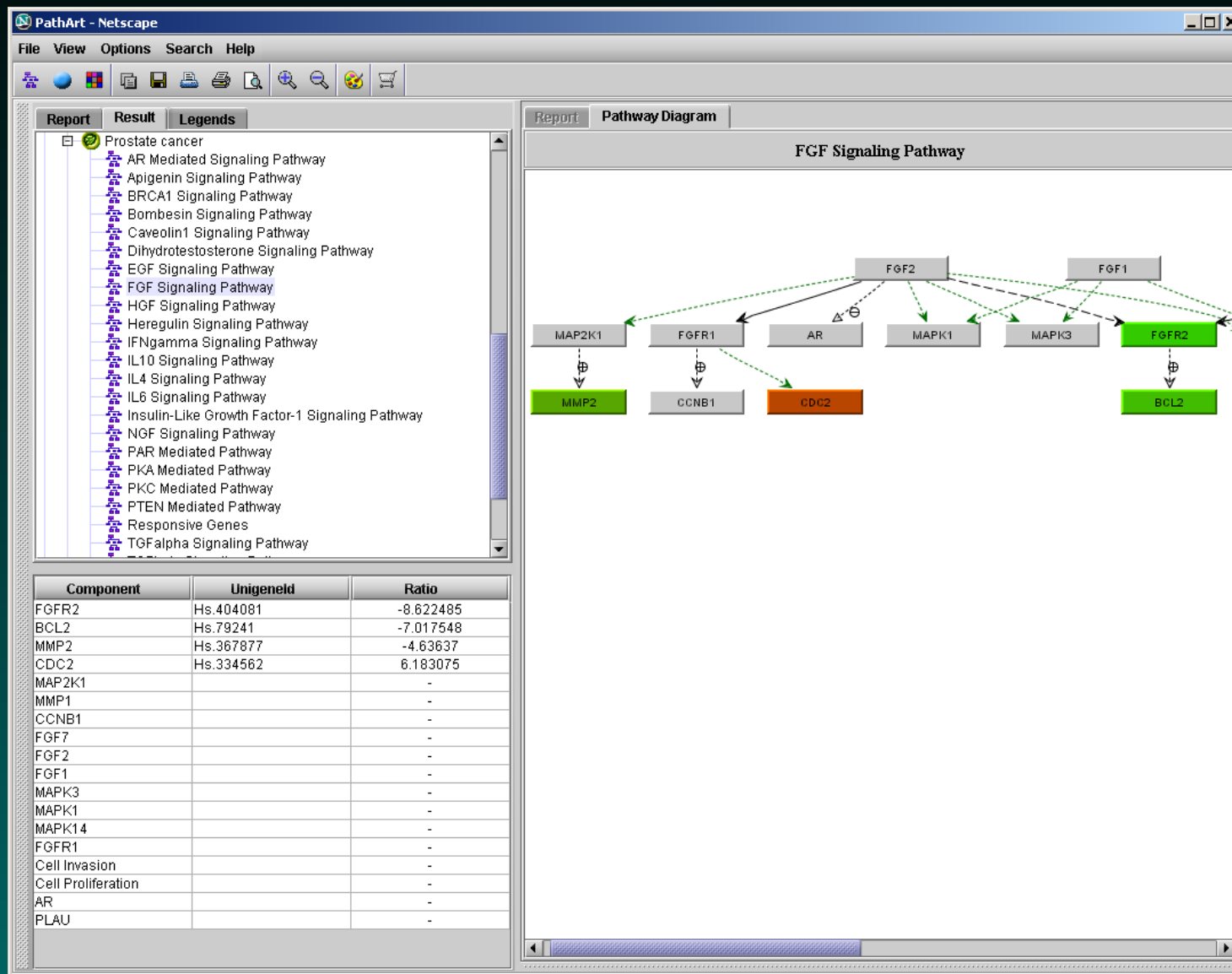
File View Options Search Help

Report Result

Cell Adhesion
Cell-cycle
Chronic Myeloid Leukemia
Colon Cancer
Development
Diabetes Type II
Growth and Differentiation
Inflammation
Keratinocyte Differentiation
Lung Cancer
Multiple Sclerosis
Myogenesis
Osteoarthritis
Osteoporosis
Others
Pancreatic Cancer
Parkinsons Disease
Prostate cancer
AR Mediated Signaling Pathway
Apigenin Signaling Pathway
BRCA1 Signaling Pathway
Bombesin Signaling Pathway
Caveolin1 Signaling Pathway
Dihydrotestosterone Signaling Pathway
EGF Signaling Pathway
FGF Signaling Pathway
HGF Signaling Pathway
Heregulin Signaling Pathway
IFNgamma Signaling Pathway
IL10 Signaling Pathway
IL4 Signaling Pathway
IL6 Signaling Pathway
Insulin-Like Growth Factor-1 Signaling Pathway
NGF Signaling Pathway
PAR Mediated Pathway
PKA Mediated Pathway
PKC Mediated Pathway
PTEN Mediated Pathway
Responsive Genes
TGFalpha Signaling Pathway
TGFbeta Signaling Pathway
TNF Signaling Pathway
TRAIL Signaling Pathway
p53 Signaling Pathway
Rheumatoid Arthritis
Reference

Organism	Physiology/Disease	Pathway	Gene Name	Gene Id
		<input type="checkbox"/> CCR5-mediated Pat...	<input type="checkbox"/> CXCL12	<input type="checkbox"/> Hs.436042
			<input type="checkbox"/> TNF	<input type="checkbox"/> Hs.241570
		<input type="checkbox"/> CD28 Mediated Path...	<input type="checkbox"/> CDK9	<input type="checkbox"/> Hs.150423
		<input type="checkbox"/> CD4-dependent Path...	<input type="checkbox"/> CXCL12	<input type="checkbox"/> Hs.436042
			<input type="checkbox"/> TNF	<input type="checkbox"/> Hs.241570
		<input type="checkbox"/> CD40L Signaling Pat...	<input type="checkbox"/> TNF	<input type="checkbox"/> Hs.241570
			<input type="checkbox"/> TNFRSF5	<input type="checkbox"/> Hs.504816
		<input type="checkbox"/> CXCR4-mediated Pa...	<input type="checkbox"/> CXCL12	<input type="checkbox"/> Hs.436042
			<input type="checkbox"/> TNF	<input type="checkbox"/> Hs.241570
		<input type="checkbox"/> Env Signaling Pathw...	<input type="checkbox"/> MYC	<input type="checkbox"/> Hs.202453
			<input type="checkbox"/> PRKCA	<input type="checkbox"/> Hs.349611
			<input type="checkbox"/> STAT3	<input type="checkbox"/> Hs.421342
	<input type="checkbox"/> Acquired Immuno Defi...	<input type="checkbox"/> LPS Signaling Path...	<input type="checkbox"/> IRAK1	<input type="checkbox"/> Hs.182018
			<input type="checkbox"/> TNF	<input type="checkbox"/> Hs.241570
		<input type="checkbox"/> Nef-mediated Pathw...	<input type="checkbox"/> STAT3	<input type="checkbox"/> Hs.421342
			<input type="checkbox"/> TNF	<input type="checkbox"/> Hs.241570
		<input type="checkbox"/> Responsive Genes	<input type="checkbox"/> MYC	<input type="checkbox"/> Hs.202453
		<input type="checkbox"/> TNFalpha Signaling ...	<input type="checkbox"/> NCOA1	<input type="checkbox"/> Hs.386092
			<input type="checkbox"/> TNF	<input type="checkbox"/> Hs.241570
		<input type="checkbox"/> Tat Signaling Pathway	<input type="checkbox"/> ITGB1	<input type="checkbox"/> Hs.287797
			<input type="checkbox"/> MAPK9	<input type="checkbox"/> Hs.348446
			<input type="checkbox"/> TNF	<input type="checkbox"/> Hs.241570
			<input type="checkbox"/> TRAF4	<input type="checkbox"/> Hs.8375
		<input type="checkbox"/> Vpr Signaling Pathw...	<input type="checkbox"/> CDC2	<input type="checkbox"/> Hs.334562
			<input type="checkbox"/> HRB2	<input type="checkbox"/> Hs.269857
			<input type="checkbox"/> TNF	<input type="checkbox"/> Hs.241570
		<input type="checkbox"/> Amyloidbeta-peptide...	<input type="checkbox"/> CDK5	<input type="checkbox"/> Hs.166071
			<input type="checkbox"/> IGF1	<input type="checkbox"/> Hs.308053
			<input type="checkbox"/> TNF	<input type="checkbox"/> Hs.241570
	<input type="checkbox"/> Alzheimers	<input type="checkbox"/> IGF1 Signaling Path...	<input type="checkbox"/> IGF1	<input type="checkbox"/> Hs.308053
		<input type="checkbox"/> Notch Signaling Pat...	<input type="checkbox"/> RBPSUH	<input type="checkbox"/> Hs.347340
			<input type="checkbox"/> CRYAB	<input type="checkbox"/> Hs.408767
		<input type="checkbox"/> Responsive Genes	<input type="checkbox"/> HSPB1	<input type="checkbox"/> Hs.76067
			<input type="checkbox"/> SERPINA3	<input type="checkbox"/> Hs.76353

The FGF pathway with array data



Weaknesses of PathArt

1. Dreadful interface

- (a) File selection box often starts blank (TAB display icons).
- (b) No easy way to return to previous screens. (Often have to reload microarray data to get back to first page.)

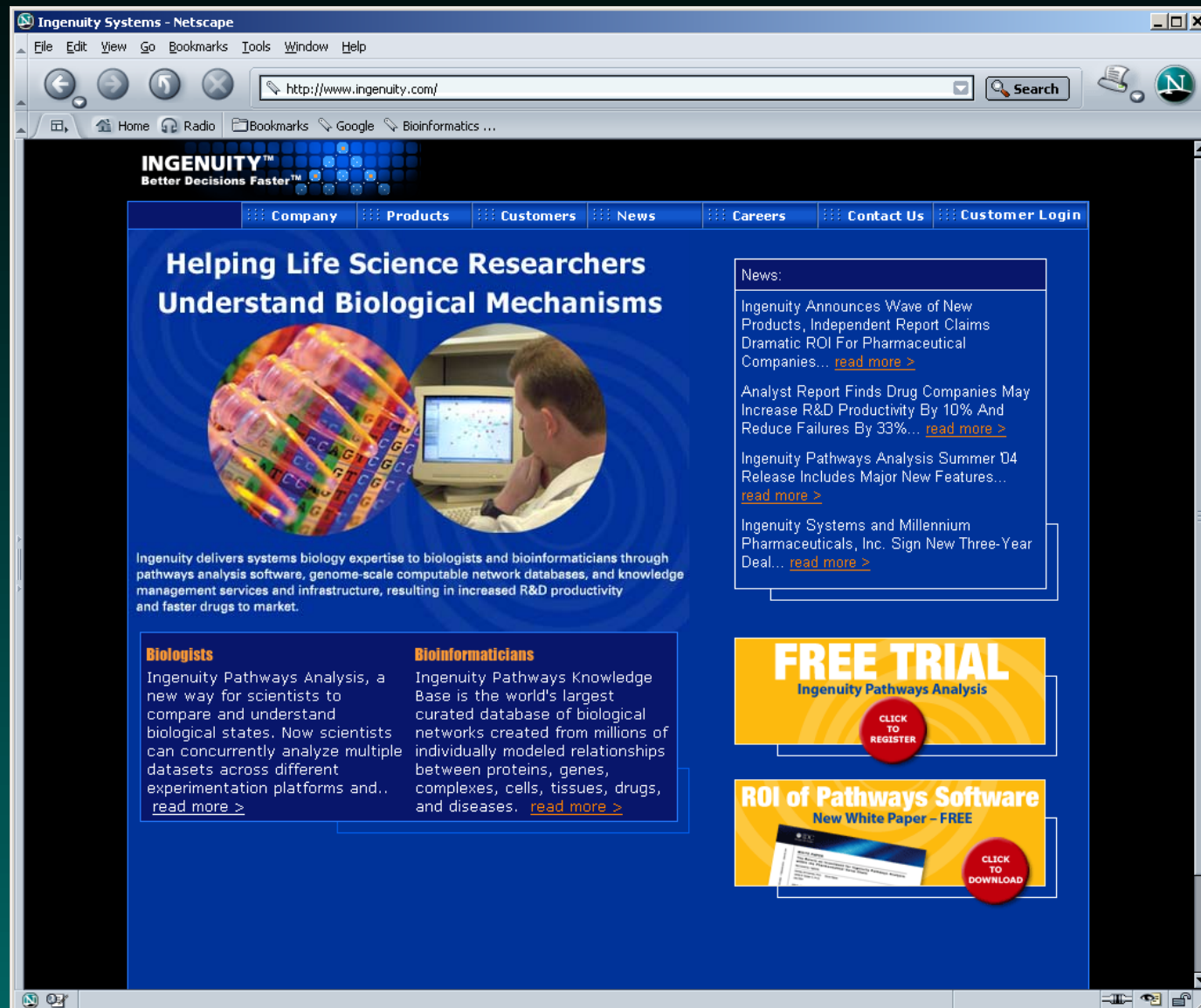
2. Diagrams are rigid

- (a) Can shrink, but not move things around
- (b) Typical diagram is wider than the screen, but not very deep
- (c) Often impossible to see all the information at once

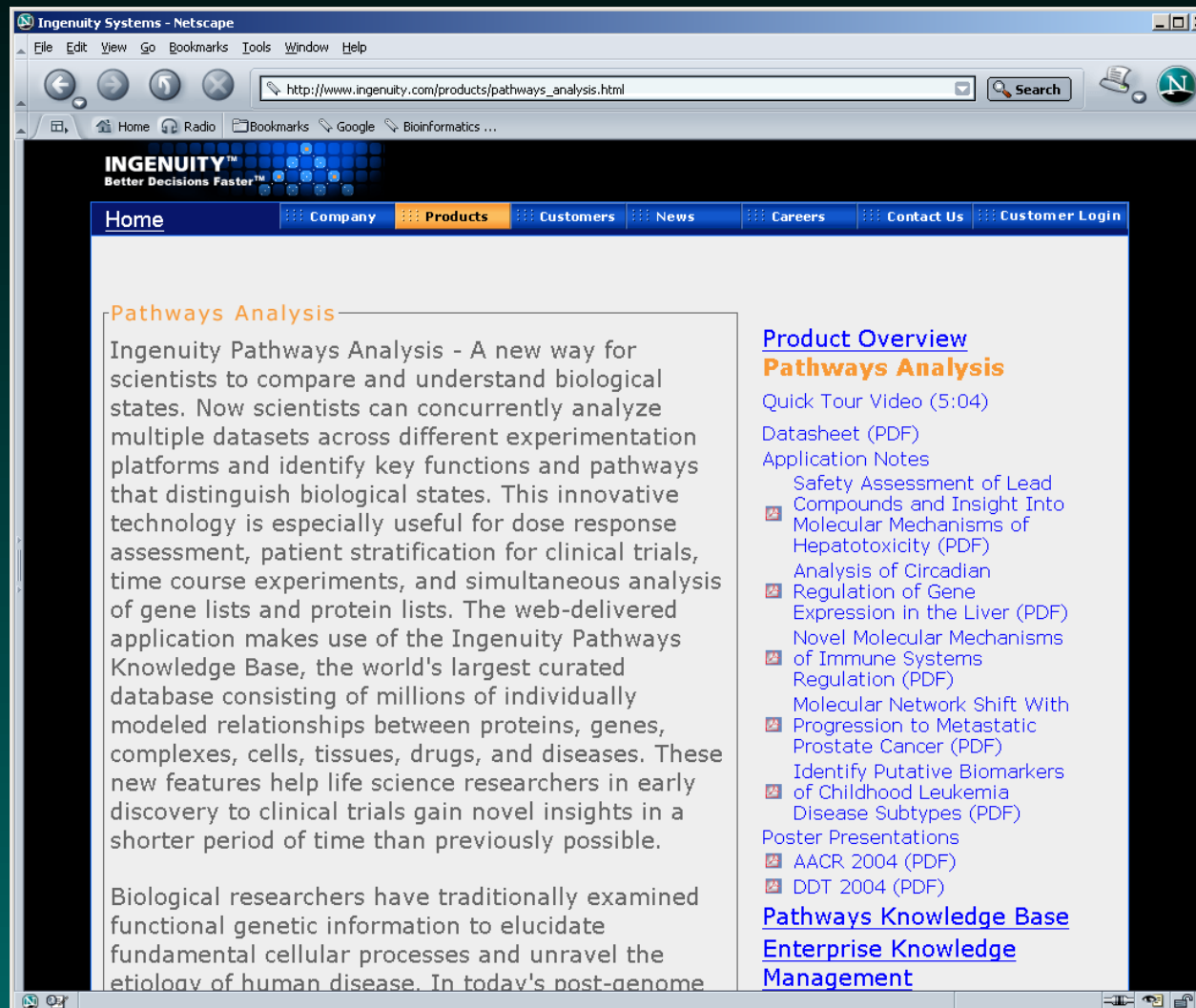
3. Cannot sort pathways by number or proportion of hits

4. No statistical way to decide if a pathway is “enriched” for differentially expressed genes

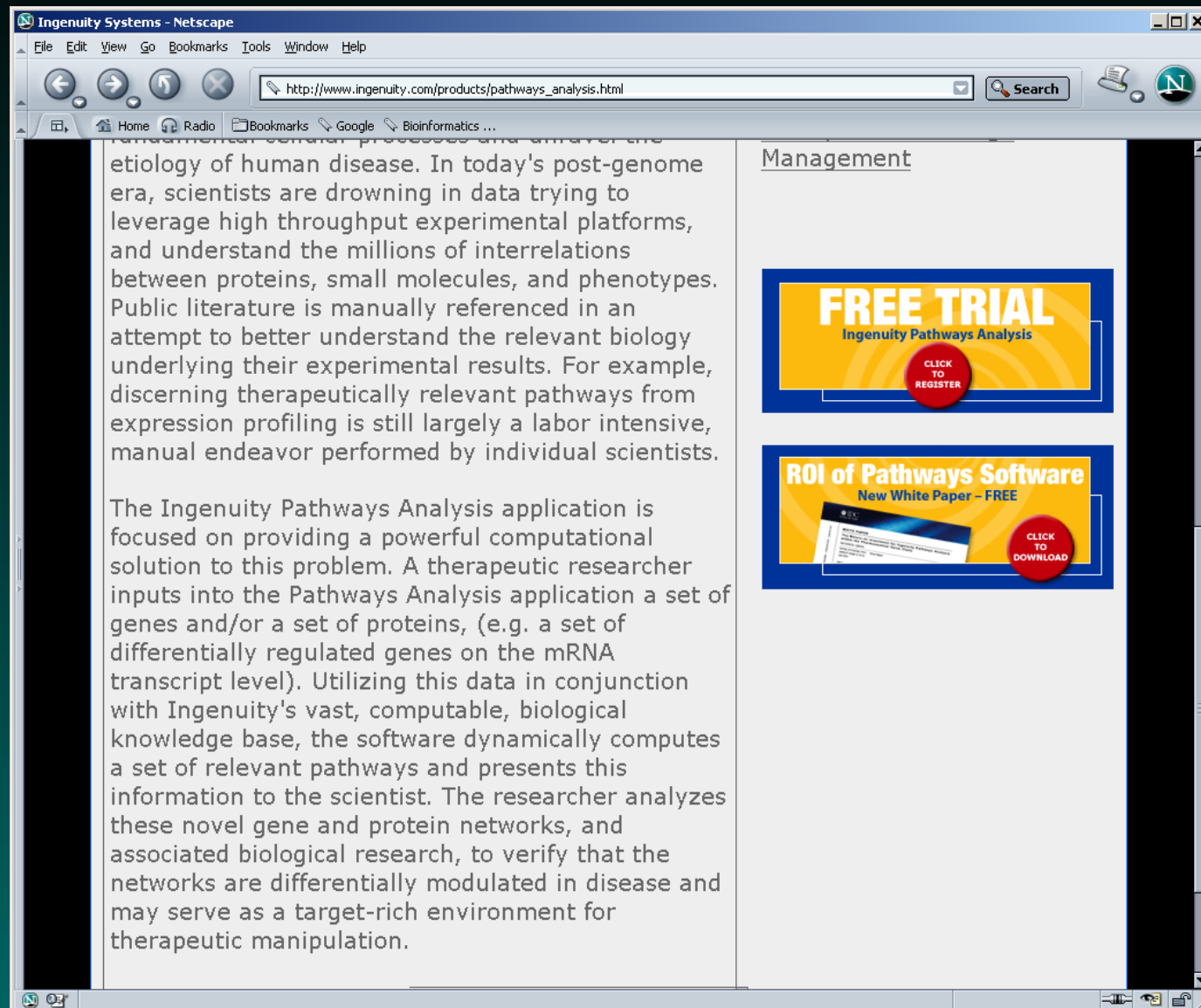
Ingenuity



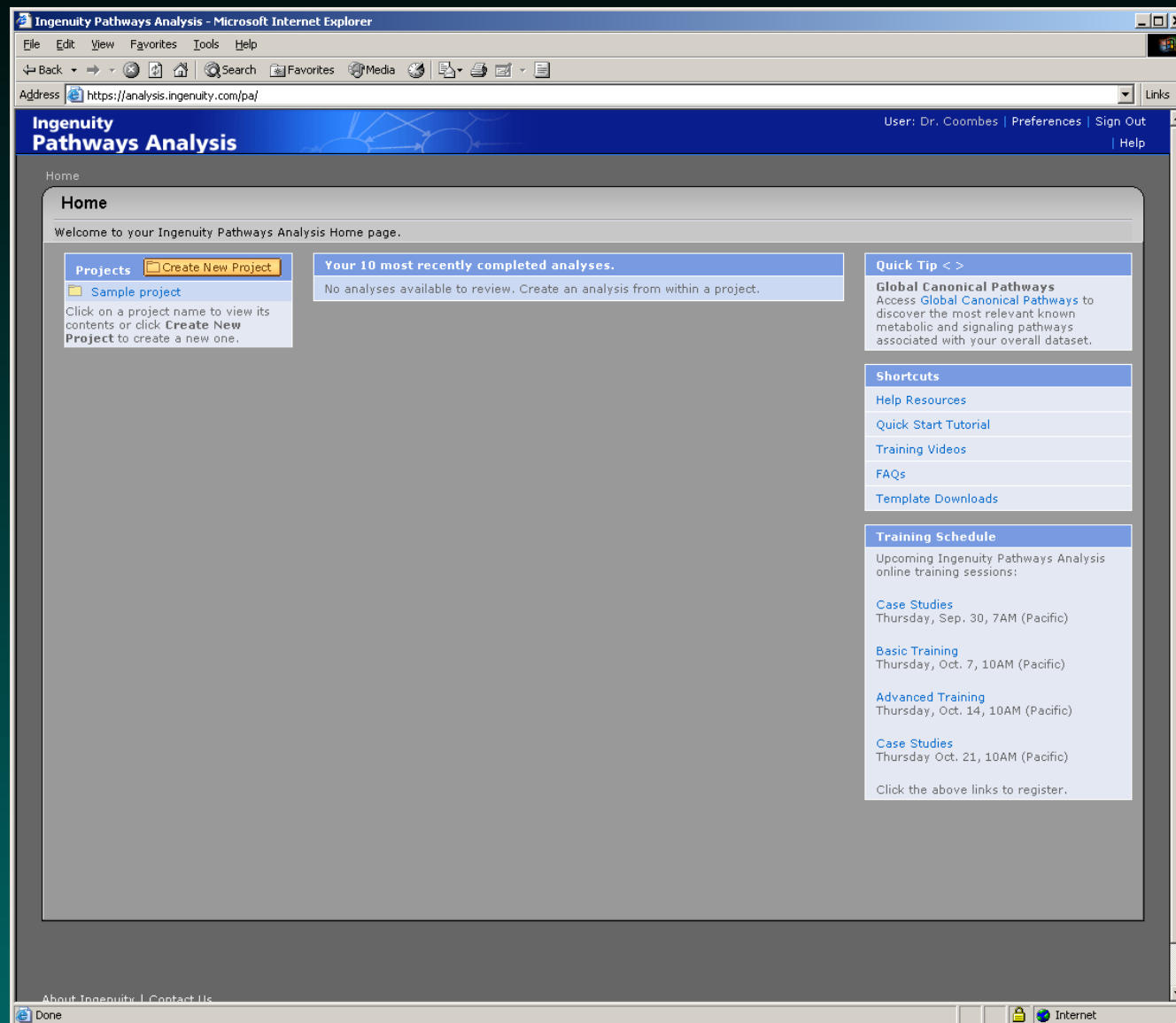
<http://www.ingenuity.com/products/pathway-analysis.html>



Ingenuity three week free trial



Ingenuity start page



Creating a new project

The screenshot shows a Microsoft Internet Explorer browser window displaying the Ingenuity Pathways Analysis website. The address bar shows the URL <https://analysis.ingenuity.com/pa/>. The page title is "Ingenuity Pathways Analysis". The user is logged in as "Dr. Coombes" and can access "Preferences", "Sign Out", "Project", and "Help" links.

The main content area is titled "Create Project" and includes the instruction: "Create a new project by completing the fields below, then click **Submit**. * Required."

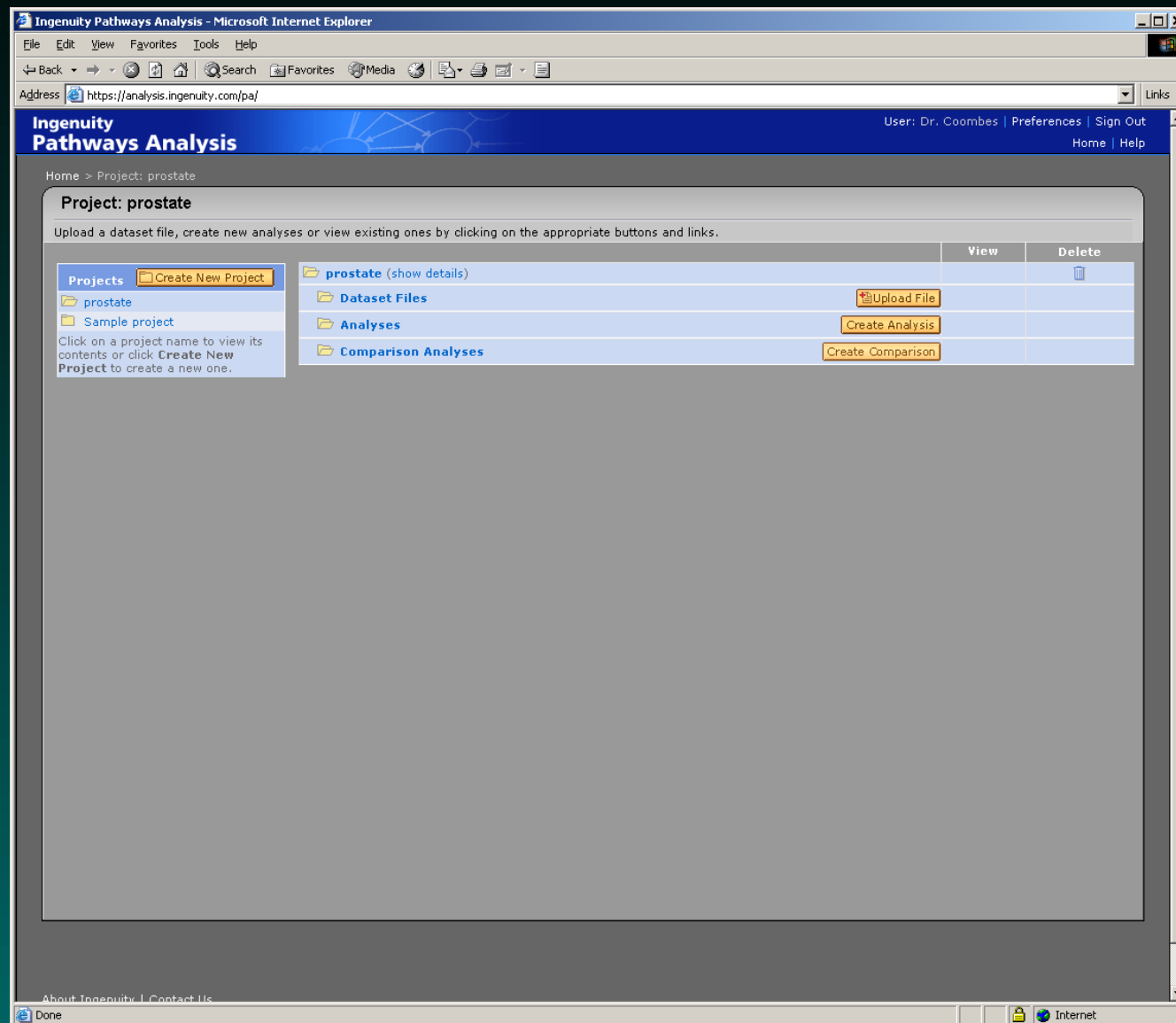
The form contains the following fields:

- Project Name:** prostate *
- Description:** t-test and tail-rank analysis of LaPointe's prostate study (400 characters maximum)
- Platform:** stanford two-color (400 characters maximum)
- Array:** stanford 42K (400 characters maximum)

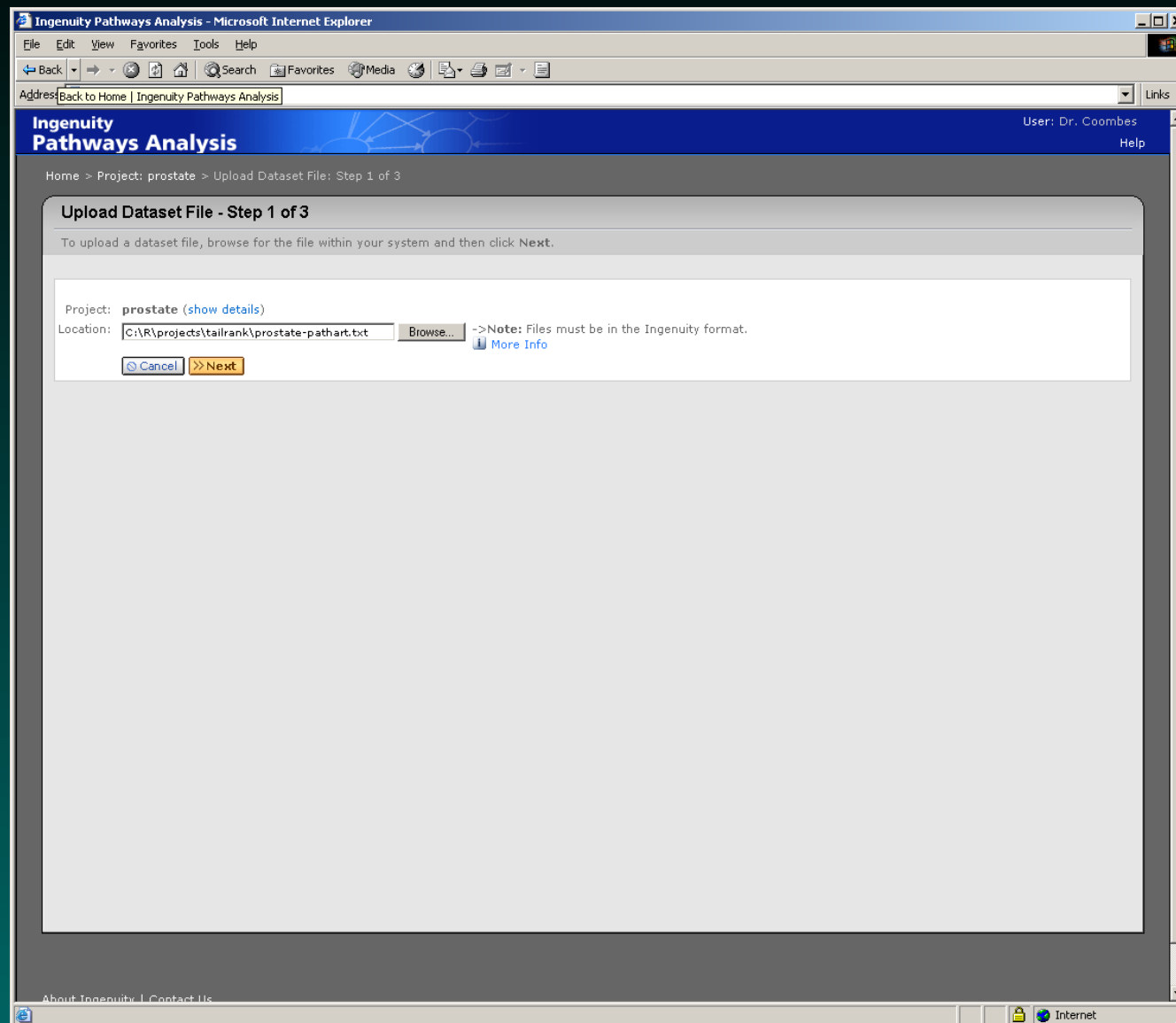
At the bottom of the form are "Cancel" and "Submit" buttons.

The footer of the page includes the text: "About Ingenuity | Contact Us" and "Copyright Ingenuity Systems 2000 - 2004 All Rights Reserved."

Ingenuity project page



Uploading microarray data



Uploading microarray data

Ingenuity Pathways Analysis - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Forward Stop Search Favorites Media Print Copy Paste

Address <https://analysis.ingenuity.com/pa/> Links »

Ingenuity Pathways Analysis User: Dr. Coombes Help

Home > Project: prostate > Upload Dataset File: Step 1 of 3 > Step 2 of 3

Upload Dataset File - Step 2 of 3

Label your dataset file, then click Next. * Required.

Project: prostate ([show details](#))

Total Number of Observations: 1 [More Info](#)
2255 row(s) detected.

File Format Detected: ☐ Ingenuity File Format A or B [More Info](#)
☒ Ingenuity Basic Format (Legacy)

Dataset File Name: prostate-pathart.txt *

Description: unigene id and t-stat for diff expr genes 400 characters maximum

[Cancel](#) [Back](#) [Next](#)

Dataset File: [prostate-pathart.txt](#)
(First 100 rows are shown below)

A: Gene/Protein ID	B: Expression Value
Cluster.ID	T.Stat
Hs.250616	-4.620291
Hs.75309	7.709446
Hs.440382	5.294954
Hs.440382	6.264828
Hs.24332	-6.522626
Hs.367688	-7.401072
Hs.272927	-8.724433
Hs.272927	-9.049278
Hs.102471	-7.192620
Hs.13604	5.809353
Hs.143251	-5.029750
Hs.48348	-5.997128
Hs.439031	-5.367195
Hs.129159	5.053361
Hs.74562	4.872108
Hs.447905	5.658341
Hs.82568	-5.931616
Hs.184298	4.320148
Hs.194662	-4.741693
Hs.8364	-6.815697
Hs.133321	-7.056189
Hs.58561	-6.367254
Hs.121576	6.288705
Hs.35380	-6.576627
Hs.449894	5.167162
Hs.42173	6.808548
Hs.102607	-5.105139
Hs.110028	-6.922639
Hs.212787	-6.415029
Hs.435733	-5.737050
Hs.136295	-7.008182

Internet

Uploading microarray data

Ingenuity Pathways Analysis - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Forward Stop Home Search Favorites Media Print Copy Paste

Address <https://analysis.ingenuity.com/pa/> Links »

Ingenuity Pathways Analysis User: Dr. Coombes Help

Home > Project: prostate > Upload Dataset File: Step 1 of 3 > Step 2 of 3 > Step 3 of 3

Upload Dataset File - Step 3 of 3

Specify the details of your dataset file, then click **Create Analysis**. * Required.

Project: prostate ([show details](#))

Dataset File Name: prostate-pathart.txt * 2255 rows imported from prostate-pathart.txt

Description: unigene id and t-stat for diff expr genes 400 characters maximum

Specify whether or not your file contains column headers and select the appropriate type of identifier and type(s) of expression values.

Contains Column Headers: Yes ☒ No ☐

Identifier Type: UniGene *

Expression Value Type: Other - normalized around zero - expected values: (-INF, +INF) * [More Info](#)

[Cancel](#) [Back](#) [Save](#) [Create Analysis](#)

Dataset File: [prostate-pathart.txt](#)
(First 100 rows are shown below)

A: Gene/Protein ID	B: Expression Value
Cluster.ID	T.Stat
Hs.250616	-4.620291
Hs.75309	7.709446
Hs.440382	5.294954
Hs.440382	6.264828
Hs.24332	-6.522626
Hs.367688	-7.401072
Hs.272927	-8.724433
Hs.272927	-9.049278
Hs.102471	-7.192620
Hs.13604	5.809353
Hs.143251	-5.029750
Hs.48348	-5.997128
Hs.439031	-5.367195
Hs.129159	5.053361
Hs.74562	4.872108
Hs.447905	5.658341
Hs.82568	-5.931616
Hs.184298	4.320148
Hs.194662	-4.741693
Hs.8364	-6.815697
Hs.133321	-7.056189
Hs.58561	-6.367254
Hs.121576	6.288705
Hs.35380	-6.576627
Hs.449894	5.167162
Hs.42173	6.808548
Hs.102607	-5.105139
Hs.110028	-6.922639
Hs.212787	-6.415029
Hs.435733	-5.737050
Hs.136295	-7.000182

Done Internet

Finding the networks (analyzing)

Ingenuity Pathways Analysis - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Forward Stop Search Favorites Media Print Copy Paste

Address <https://analysis.ingenuity.com/pa/> Links >>

Ingenuity Pathways Analysis User: Dr. Coombes Help

Home > Project: prostate > Create Analysis - Step 1 of 2

Create Analysis - Step 1 of 2

Label your analysis, select a dataset file and then click Next. * Required.

Project: prostate ([show details](#))

Analysis Name: prostate DE *

Description: find pathways containing diff expr prostate genes 400 characters maximum

Select Dataset File: prostate

Dataset Files

☒ prostate-pathart.txt

Done Internet

Finding the networks (analyzing)

Ingenuity Pathways Analysis - Microsoft Internet Explorer

Address: <https://analysis.ingenuity.com/pa/>

User: Dr. Coombes Help

Home > Project: prostate > Create Analysis - Step 1 of 2 > Step 2 of 2

Create Analysis - Step 2 of 2

Define and review analysis parameters, review identifier mapping and then click **Run Analysis**. * Required.

Project: prostate ([show details](#))

Analysis Name: prostate DE *

Description: find pathways containing diff expr prostate genes 400 characters maximum

Number of Identifiers in File: 2254 identifiers in [prostate-pathart.txt](#)

Define network focus genes and global analysis genes

Expression Value Cutoff		Focus On
Exp Val Type 1	Other: <input type="text"/> Range -14.427 to 14.122	<input checked="" type="radio"/> Both Up/Downregulated Identifiers <input type="radio"/> Upregulated Identifiers <input type="radio"/> Downregulated Identifiers

[Recalculate](#)

589 genes eligible for generating networks

[More Info](#)
([view Dataset File Mapping](#))

[Cancel](#) [Back](#) [Run Analysis](#) [Advanced Settings \(show details\)](#)

Observations Selected for Analysis [More Info](#)

Select Observations	Network Focus Genes	Global Analysis Genes
<input checked="" type="checkbox"/> prostate DE	589	753

Dataset File Mapping [show details](#)

About Ingenuity | Contact Us
Copyright Ingenuity Systems 2000 - 2004 All Rights Reserved.

Done Internet

Waiting for the analysis to complete

Ingenuity Pathways Analysis - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Forward Stop Search Favorites Media Print Copy Paste

Address <https://analysis.ingenuity.com/pa/> Links »

Ingenuity Pathways Analysis User: Dr. Coombes | Preferences | Sign Out | Home | Help

Home > Project: prostate

Project: prostate

Upload a dataset file, create new analyses or view existing ones by clicking on the appropriate buttons and links.

Projects [Create New Project](#)

- prostate
- Sample project

Click on a project name to view its contents or click [Create New Project](#) to create a new one.

	View	Delete
prostate (show details) Dataset Files prostate-pathart.txt (show details) Upload File	File	
Analyses prostate DE (show details) Create Analysis	Running	
Comparison Analyses Create Comparison		

Done Internet

Ingenuity networks

Ingenuity Pathways Analysis - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Address <https://analysis.ingenuity.com/pa/>

User: Dr. Coombes | Preferences | Sign Out
Dataset File Mapping | Project | Help

Home > Project Manager > Analysis Summary

Analysis Summary: prostate DE (show details)

To view a network, click on the icon in the Network Explorer column. To merge networks, select the appropriate checkboxes and click Merge.

Networks (77) Global Functions & Pathways Gene by Gene View Search

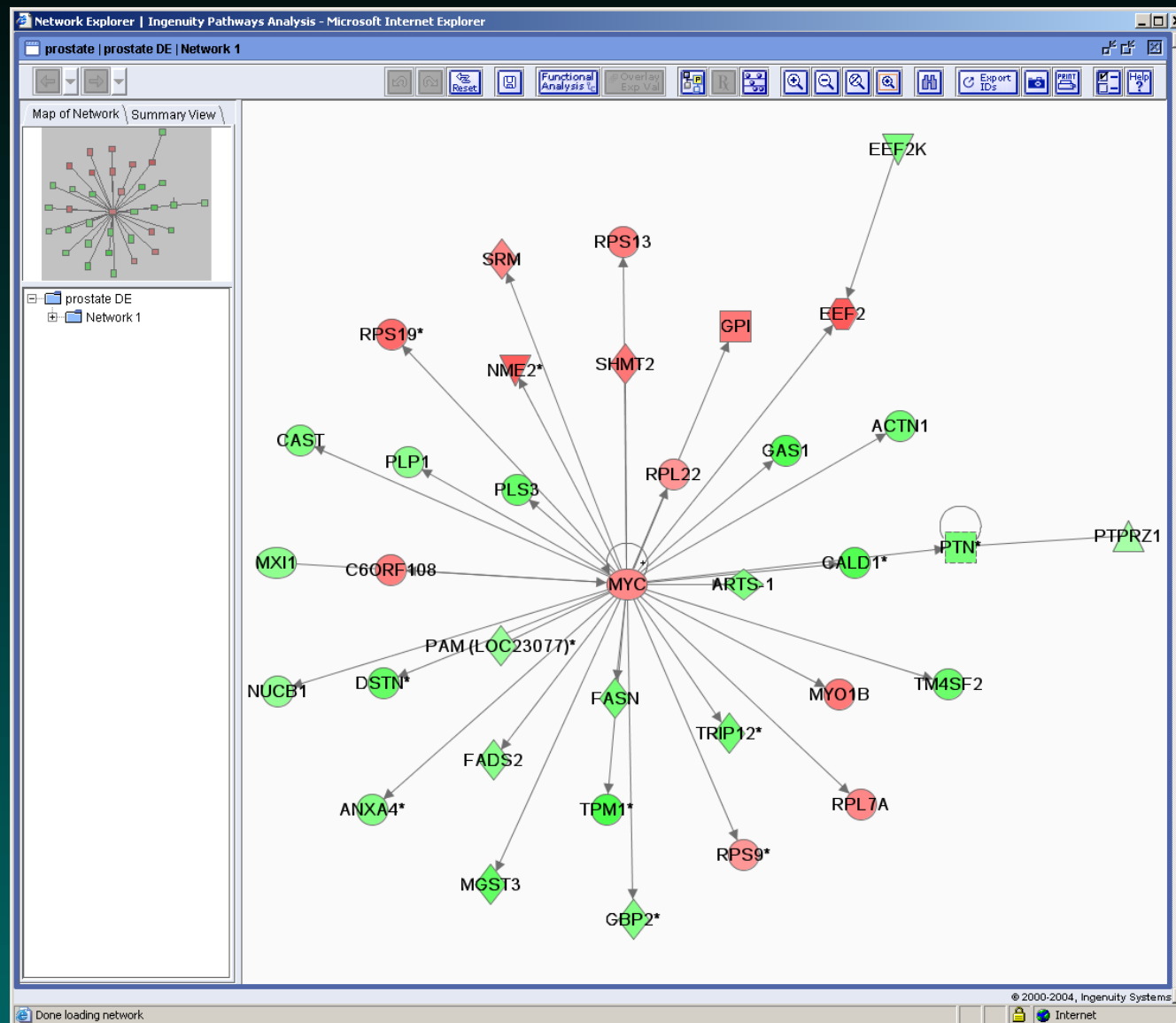
List of Networks | **Overlapping Networks** | Merged Networks

Networks 1 to 50 of 77 [Export All](#) [Click to view your merged networks](#) Previous | Next 27 >> Show Network ID 1 - 50

Network ID	Genes in Network	Network Explorer	Score	#Focus Genes	Top Functions	Merge
1	ACTN1, ANXA4, ARTS-1, C6ORF108, CALD1, CAST, DSTN, EEF2, EEF2K, FADS2, FASN, GAS1, GBP2, GPI, MGST3, MXI1, MYC, MYO1B, NME2, NUCB1, PAM (LOC23077), PLP1, PLS3, PTN, PTPRZ1, RPL22, RPL7A, RPS13, RPS19, RPS9, SHMT2, SRM, TM4SF2, TPM1, TRIP12		37	35	Cancer, Protein Synthesis, Cellular Movement. View all	<input type="checkbox"/>
2	BCOR, COX5A, DNMT3A, DUSP3, EVI1, FHL1, FOSL2, HDAC1, IFRD1, JUNB, KIAA0601, MADH3, MAF, MAP2K7, MAP3K1, MAPK8IP3, MAPK9, MAPKAPK3, MEI51, MEI52, MYLK, NFE2L2, PAK1, PAK1IP1, PBX1, PPARG, PPARGC1A, PRNP, RARB, RARG, RBPSUH, SH3MD2, SIN3B, SLC2A4, SMARCA3		37	35	Gene Expression, Organismal Development, Skeletal and Muscular System Development and Function. View all	<input type="checkbox"/>
3	ACVR2B, CAV1, CAV2, CD47, CD9, EDG1, EGFR, F2R, FNBP1, GJA1, GJB1, IGSF8, IL6ST, ITGA1, ITGA2, ITGB1, LEPR, MET, OCLN, PPAP2B, PRKCA, PTGFRN, PTPN11, PTPNS1, SLC7A6, SNX1, SNX2, STAT3, TGFA, TGFBR2, TGFBR3, TGFBR4, TGFBR5, VAV3		37	35	Cellular Movement, Cellular Growth and Proliferation, Cancer. View all	<input type="checkbox"/>
4	APOE, ATP2A2, B2M, BAF53A, BCL2, BNIP3L, CDX2, CXCL12, FKBP4, GRP58, HFE, KLK3, LGALS3, LGALS3BP, MITE, MMP2, NID, NR3C1, PLN, POMC, PPIC, RTN4, RUVBL1, SERPINA3, SMARCC1, SMARCD2, SMARCD3, STAT5B, TCF4, TIMP2, TIMP3, TNF, TRA1, TRRAP, ZNF270		37	35	Hematological System Development and Function, Immune and Lymphatic System Development and Function, Tissue Development. View all	<input type="checkbox"/>
5	ANXA1, ANXA2, ARHB, CDC2, CDK4, CDK5, CDK7, CDK9, CDKN1B, CTSB, CUL1, DAPK1, FBXO32, FMR1, FOXD1A, HES1, ID3, IFI16, IRF2, MSN, NEDD8, NEFH, PPP1R12A, PPP1R12B, PPP3CA, PRKCL1, ROCK2, S100A10, SFN, SKP1A, SLPI, TOPK, TP73L, VIM, YAP1		37	35	Cell Cycle, Cellular Development, Cardiovascular Disease. View all	<input type="checkbox"/>
6	AMOT, CPE, CPEB1, DDEF1, EPAS1, EPHB1, ERBB2, ERBB4, F2, F5, GP120, GP80, GRB7, HIF1A, NRG1, NR1, NRP2, PARVA, PLG, PXN, RAS1, RNF41, SDFR1, SEMA3A, SEMA3C, SEMA3D, SEMA3E, SEMA3F, SERPINF2, SOCS4, STK6, TCEB1, VEGF, W5B1, W5B2		11	19	Cellular Compromise, Neurological Disease, Cell-To-Cell Signaling and Interaction. View all	<input type="checkbox"/>
7	ACTA1, ACTA2, ACTB, ACTC, ACTG1, ACTG2, CAPG, CCT2, CCT3, CCT4, CCT5, CCT6A, CCT7, CCT8, CDC104, CDC42, CDC42EP3, CDC42EP5, CNN1, GSN, MYC, MYO6, PAK3, PARD6G, PIP5K1A, RAB27A, RAC1, RSN, SEPT6, STX1A, SWAP70, SYTL4, TC10, TIAM1, WASP, WASPIP		10	18	Cellular Assembly and Organization, Cellular Function and Maintenance. View all	<input type="checkbox"/>

<https://analysis.ingenuity.com/pa/networkview/networkview.jsp?view=6&show=6&sort=3&order=1>

The first network: MYC



Ingenuity figure legend

Ingenuity Pathways Analysis Help - Microsoft Internet Explorer

Contents Index Search Glossary

Search - Go Ingenuity

Legend

This legend provides an key of the main features of Network Explorer and Canonical Pathways, including node shapes and colors as well as edge labels and types. For details, see [Network Explorer](#) and [Canonical Pathways](#).

Network Explorer & Canonical Pathways Node Shapes

Network Explorer Node Shapes

Canonical Pathways Node Shapes

Network Explorer & Canonical Pathways Edges

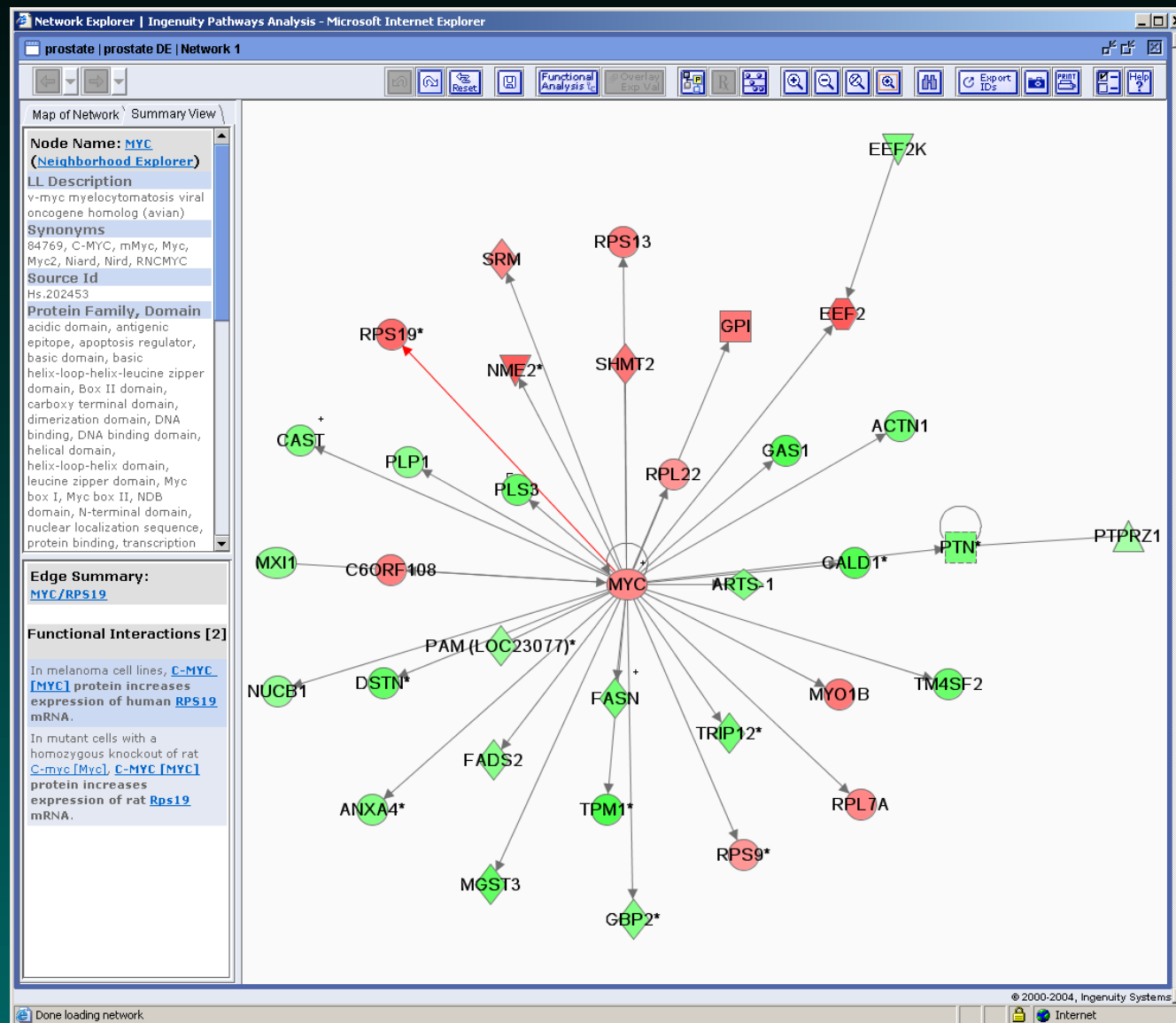
Network Explorer Edge Types

Canonical Pathways Edge Types

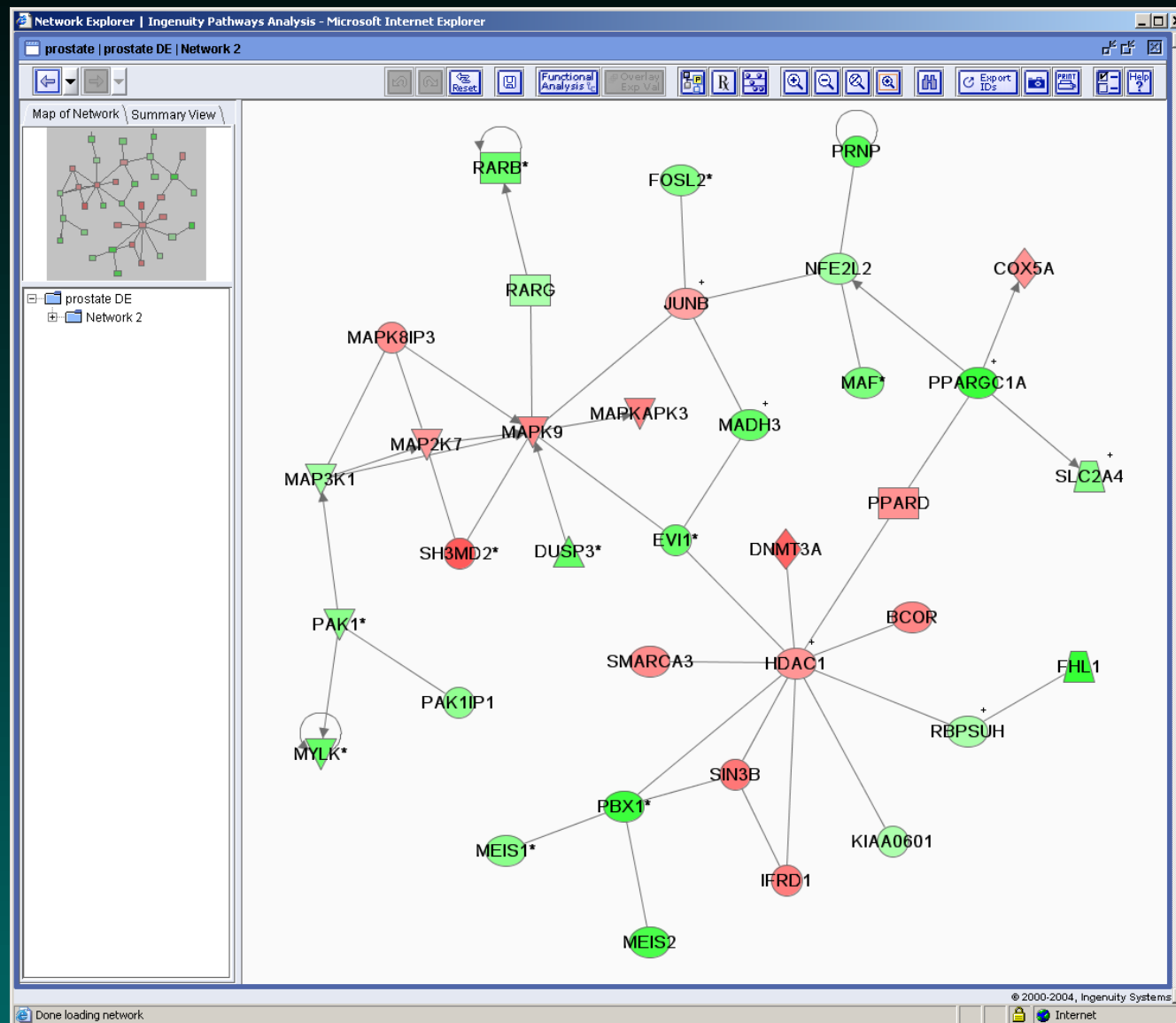
Edge Labels

Edge Label	Description
A	Activation/deactivation
B	Binding
E	Expression
I	Inhibition
L	proteoLysis
M	biochemical Modification
O	Other
P	Phosphorylation/dephosphorylation
T	Transcription

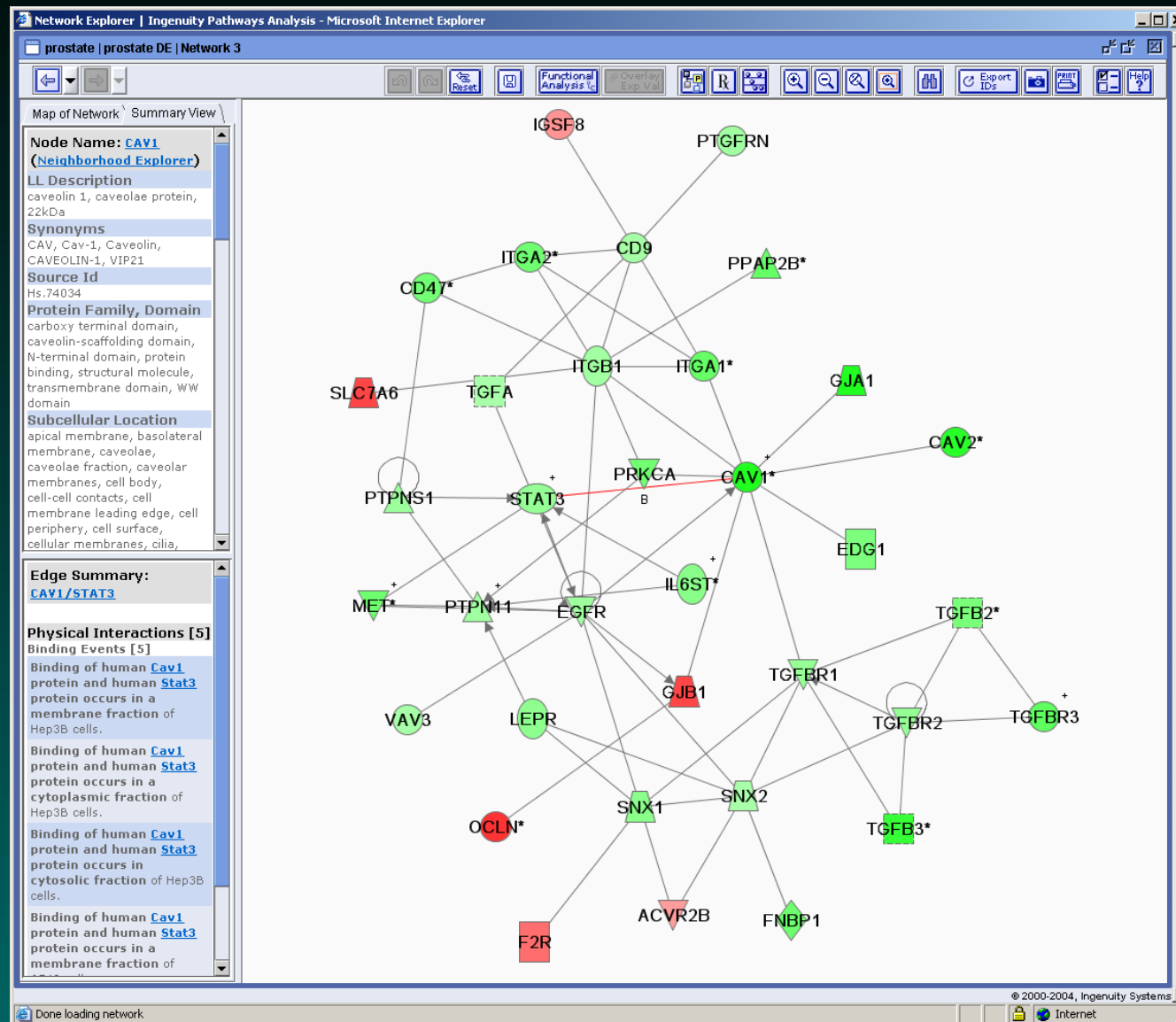
Evidence for interactions



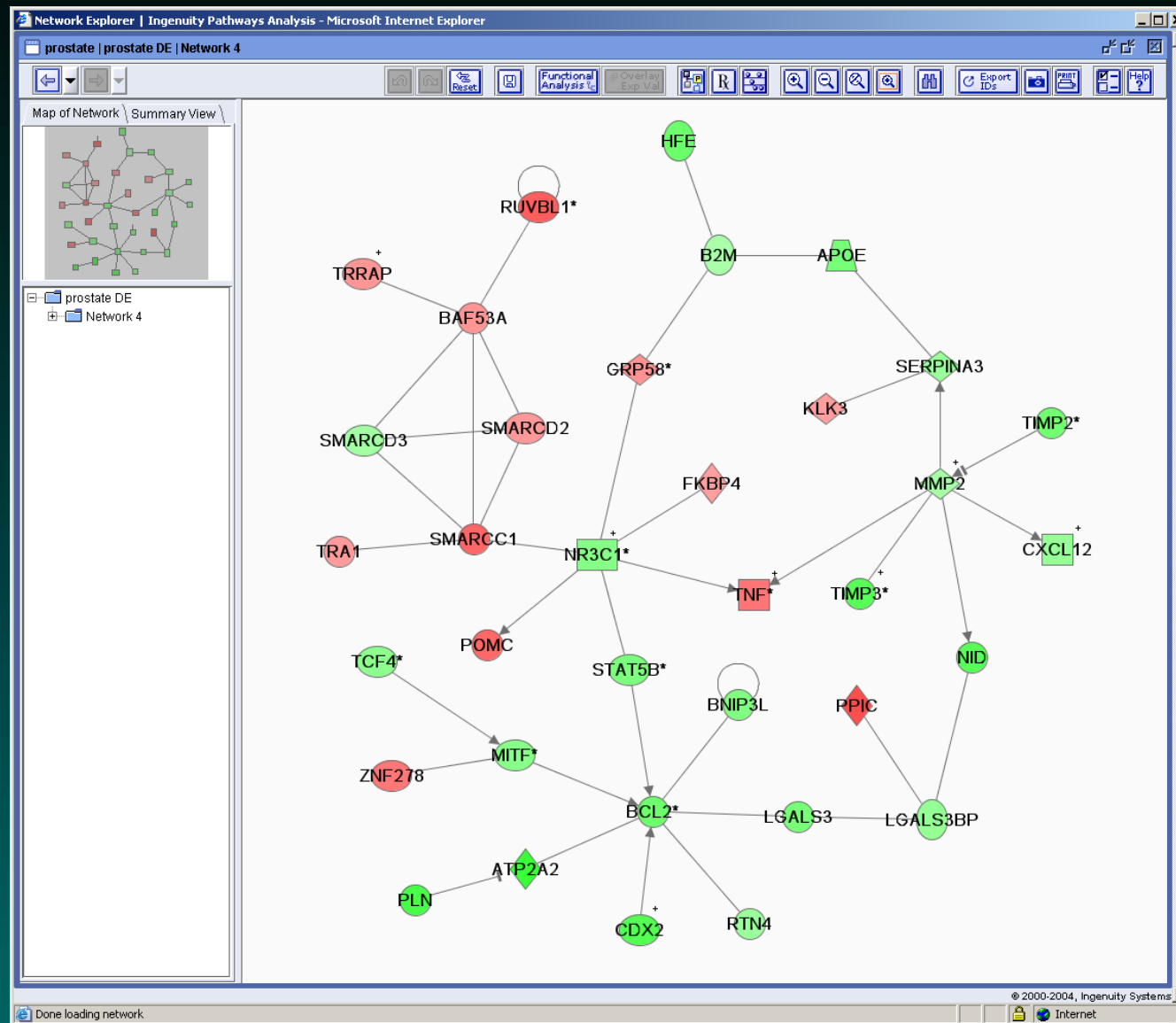
Second network



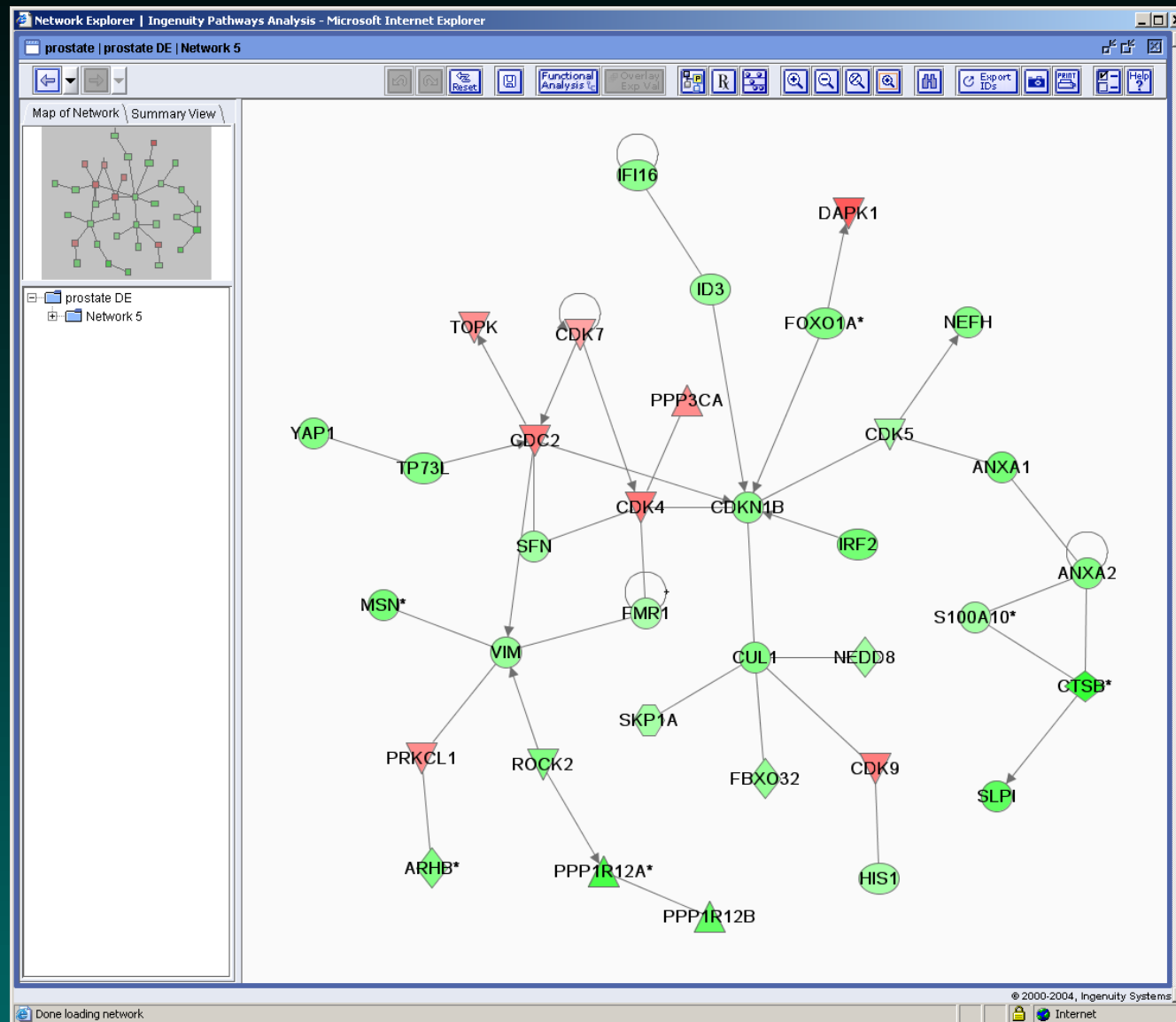
Third network



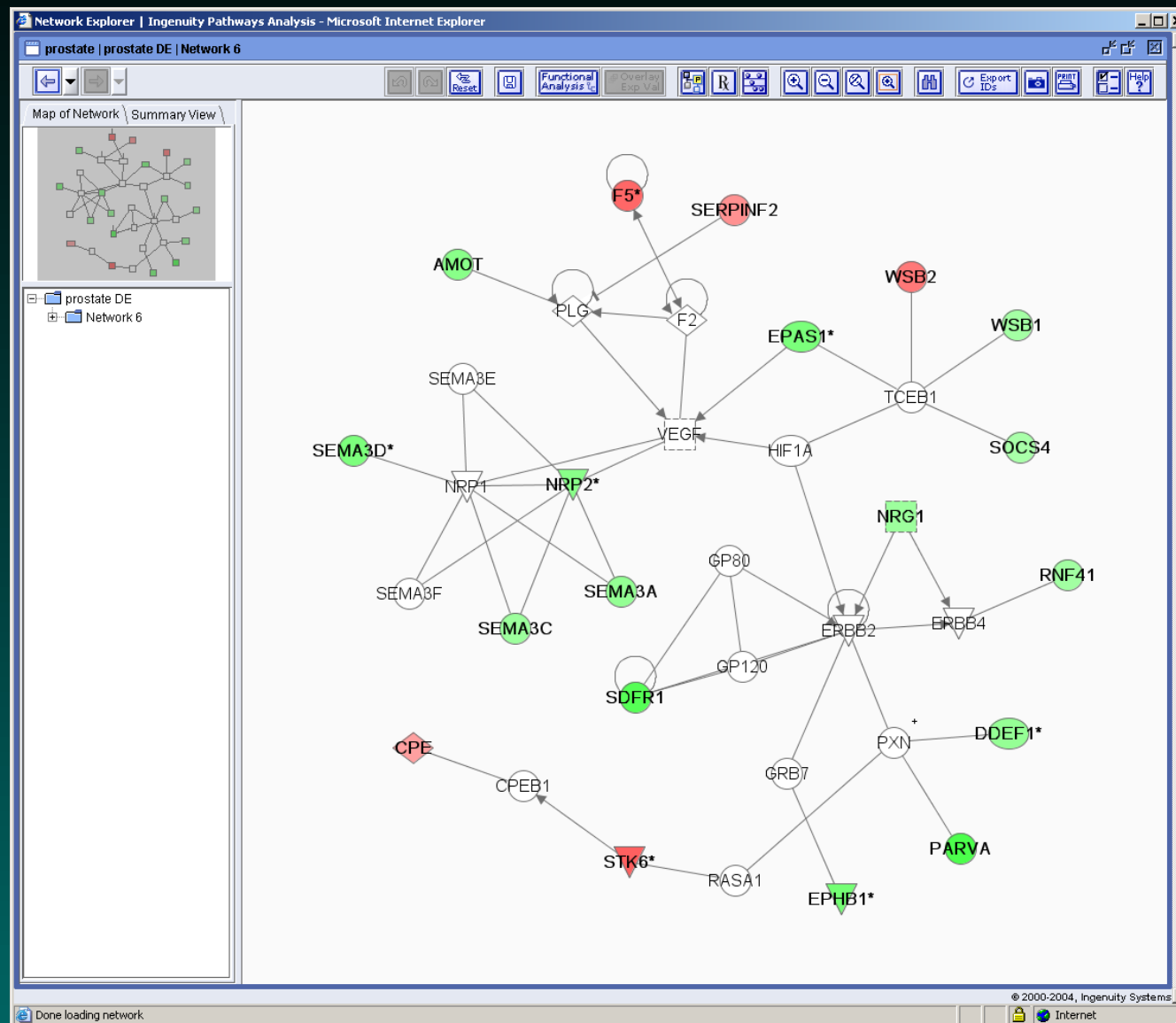
Fourth network



Fifth network



Sixth network



CAV1 node details

Node View: CAV1 | Ingenuity Pathways Analysis - Microsoft Internet Explorer

Address: <https://analysis.ingenuity.com/pa/nodeview/nodeview.jsp?nodeid=947648223&analysisid=31151&profileid=467524>

User: Dr. Coombes

Help

Node View: CAV1

Node View: CAV1 (Neighborhood Explorer)

Review the categorized literature findings and database information for this node.

CAV1 Human Mouse Rat

LL Description:	caveolin 1, caveolae protein, 22kDa
Synonyms:	CAV, Cav-1, Caveolin, CAVEOLIN-1, VIP21
Source Id:	Hs.74034
Protein Family, Domain:	carboxy terminal domain, caveolin-scaffolding domain, N-terminal domain, protein binding, structural molecule, transmembrane domain, WW domain
Subcellular Location:	apical membrane, basolateral membrane, caveolae, caveolae fraction, caveolar membranes, cell body, cell-cell contacts, cell membrane leading edge, cell periphery, cell surface, cellular membranes, cilia, cytoplasm, cytoplasmic foci, cytoplasmic fraction, cytoplasmic vesicles, cytosolic fraction, detergent-insoluble fractions, detergent-insoluble membrane fraction, detergent insoluble microdomains, Golgi apparatus, Golgi apparatus component, growth cone, membrane fraction, membrane rafts, microvilli, neuronal varicosities, pericentrosomal region, perijunctional region, perinuclear Golgi regions, perinuclear region, plasma membrane, plasma membrane fraction, raft fractions, soluble fraction, trans Golgi network, transverse tubules, vesicles

Top findings from Ingenuity Knowledge Base (show all 1453 categorized literature findings)

regulates:	Akt, ALB, CAV1, CAV2, CCND1, CTNNB1, FOLR1, FYN, GJB2, GLB1, GSK3B, Integrin protein, LCK, MAPK1, MAPK3
regulated by:	ABL1, ACP1, AGT, APOA1, Calmodulin, CAV1, CAV2, CCK, COL18A1, CRK, CSK, CYTOTOXIC NECROTIZING FACTOR, E6, EGF, EGFR
binds:	ACP1, Adenylyl Cyclase, ADRBK1, APOA1, AR, ARHA, BENE, CAV2, CD4, CDH1, CSK, CTNNB1, CX36, DAG1, Dynamin
role in cell:	apoptosis, assembly, cell stage, colony formation, degeneration, developmental process, diameter, formation, invasion, morphology
disease:	cancer, cardiovascular disease, skeletomuscular disorder

Descriptions from External Databases

LocusLink Summary:	The scaffolding protein encoded by this gene is the main component of the caveolae plasma membranes found in most cell types. The protein links integrin subunits to the tyrosine kinase FYN, an initiating step in coupling integrins to the Ras-ERK pathway and promoting cell cycle progression. The gene is a tumor suppressor gene candidate and a negative regulator of the Ras-p42/44 MAP kinase cascade. CAV1 and CAV2 are located next to each other on chromosome 7 and express colocalizing proteins that form a stable hetero-oligomeric complex. By using alternative initiation codons in the same reading frame, two isoforms (alpha and beta) are encoded by a single transcript from this gene.
---------------------------	--

GO Annotations

Molecular Function:	structural molecule activity
Biological Process:	--
Cellular Component:	integral to plasma membrane; caveolar membrane

1453 Categorized Literature Findings (show details)

Links to the literature are harder to find

The screenshot shows the Ingenuity Pathways Analysis web interface in a Microsoft Internet Explorer browser. The address bar displays the URL: https://analysis.ingenuity.com/pa/nodeview/findings.jsp?hname=Functional%20Roles&sname=Molecular%20Processes&cname=expression+of&gname=cav1_ortholog&analysisid=31151&factgroup=CAV2. The page title is "Findings | Ingenuity Pathways Analysis - Microsoft Internet Explorer".

The main content area is titled "Findings: Functional Roles" and includes a sub-header "Node View: CAV1 > Functional Roles". Below this, there is a section for "Findings 1 - 4 of 4" with an "Expand All" button. The findings are listed as follows:

- ☐ **CAVEOLIN1 [CAV]** protein increases the expression of mouse **Caveolin-2 [Cav2]** protein in cultured fibroblasts from embryonic mouse that is decreased by mutant mouse **Caveolin-1 [Cav]** gene (homozygous knockout) in mouse.
 11457855 Razani B, Engelman JA, Wang XB, Schubert W, Zhang XL, Marks CB, Macaluso F, Russell RG, Li M, Pestell RG, Di Vizio D, Hou H, Kneitz B, Lagaud G, Christ GJ, Edelman W, Lisanti MP. Caveolin-1 null mice are viable but show evidence of hyperproliferative and vascular abnormalities. J Biol Chem 2001 Oct 12;276(41):38121-38.
- ☐ Mutant mouse **Cav-1 [Cav]** gene (homozygous knockout) in mouse decreases expression of mouse **Caveolin-2 [Cav2]** protein in mouse Mef cells.
- ☐ Mutant mouse **Caveolin-1 [Cav]** gene (homozygous knockout) in mouse decreases expression of mouse **Caveolin-2 [Cav2]** protein in cultured fibroblasts from embryonic mouse.
- ☐ In mouse, mutant mouse **Caveolin 3 [Cav3]** gene (homozygous knockout) and mutant mouse **Caveolin-1 [Cav]** gene (homozygous knockout) decrease expression of mouse **Caveolin-2 [Cav2]** protein.

At the bottom of the page, there is a footer with the text: "About Ingenuity | Contact Us Copyright Ingenuity Systems 2000 - 2004 All Rights Reserved."

Links to literature are live

Entrez PubMed - Microsoft Internet Explorer

Address: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11457855&dopt=Abstract

NCBI PubMed National Library of Medicine NLM

Entrez PubMed Nucleotide Protein Genome Structure OMIM PMC Journals Books

Search PubMed for [] Go Clear

Limits Preview/Index History Clipboard Details

Display: Abstract Show: 20 Sort: Send to: Text

1: J Biol Chem. 2001 Oct 12;276(41):38121-38. Epub 2001 Jul 16. [Related Articles, Links](#)

[FREE full text article at www.jbc.org](#)

Caveolin-1 null mice are viable but show evidence of hyperproliferative and vascular abnormalities.

Razani B, Engelman JA, Wang XB, Schubert W, Zhang XL, Marks CB, Macaluso F, Russell RG, Li M, Pestell RG, Di Vizio D, Hou H Jr, Kneitz B, Lagaud G, Christ GJ, Edelmann W, Lisanti MP.

Department of Molecular Pharmacology and The Albert Einstein Cancer Center, The Albert Einstein College of Medicine, Bronx, New York 10461, USA.

Caveolin-1 is the principal structural protein of caveolae membranes in fibroblasts and endothelia. Recently, we have shown that the human CAV-1 gene is localized to a suspected tumor suppressor locus, and mutations in Cav-1 have been implicated in human cancer. Here, we created a caveolin-1 null (CAV-1 ^{-/-}) mouse model, using standard homologous recombination techniques, to assess the role of caveolin-1 in caveolae biogenesis, endocytosis, cell proliferation, and endothelial nitric-oxide synthase (eNOS) signaling. Surprisingly, Cav-1 null mice are viable. We show that these mice lack caveolin-1 protein expression and plasmalemmal caveolae. In addition, analysis of cultured fibroblasts from Cav-1 null embryos reveals the following: (i) a loss of caveolin-2 protein expression; (ii) defects in the endocytosis of a known caveolar ligand, i.e. fluorescein isothiocyanate-albumin; and (iii) a hyperproliferative phenotype. Importantly, these phenotypic changes are reversed by recombinant expression of the caveolin-1 cDNA. Furthermore, examination of the lung parenchyma (an endothelial-rich tissue) shows hypercellularity with thickened alveolar septa and an increase in the number of vascular endothelial growth factor receptor (Flk-1)-positive endothelial cells. As predicted, endothelial cells from Cav-1 null mice lack caveolae membranes. Finally, we examined eNOS signaling by measuring the physiological response of aortic rings to various stimuli. Our results indicate that eNOS activity is up-regulated in Cav-1 null animals, and this activity can be blunted by using a specific NOS inhibitor, nitro-L-arginine methyl ester. These findings are in accordance with previous in vitro studies showing that caveolin-1 is an endogenous inhibitor of eNOS. Thus, caveolin-1 expression is required to stabilize the caveolin-2 protein product, to mediate the caveolar endocytosis of specific ligands, to negatively regulate the proliferation of certain cell types, and to provide tonic inhibition of eNOS activity in endothelial cells.

PMID: 11457855 [PubMed - indexed for MEDLINE]

Display: Abstract Show: 20 Sort: Send to: Text

Internet

Ingenuity statistical information

