

geneXplain

BioUML – open source integrated platform for collaborative and reproducible research in systems biology

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www.biouml.org

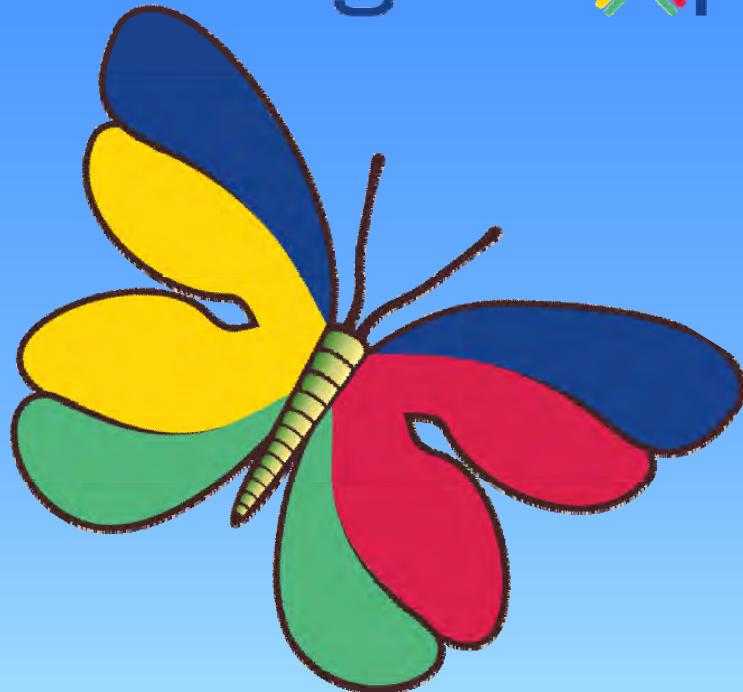
BioUML platform

- BioUML is an open source integrated platform for systems biology that spans the comprehensive range of capabilities including access to databases with experimental data, tools for formalized description, visual modeling and analyses of complex biological systems.
- Due to scripts (R, JavaScript) and workflow support it provides powerful possibilities for analyses of high-throughput data.
- Plug-in based architecture (Eclipse run time from IBM is used) allows to add new functionality using plug-ins.

BioUML platform consists from 3 parts:

- BioUML server – provides access to biological databases;
- BioUML workbench – standalone application.
- BioUML web edition – web interface based on AJAX technology;

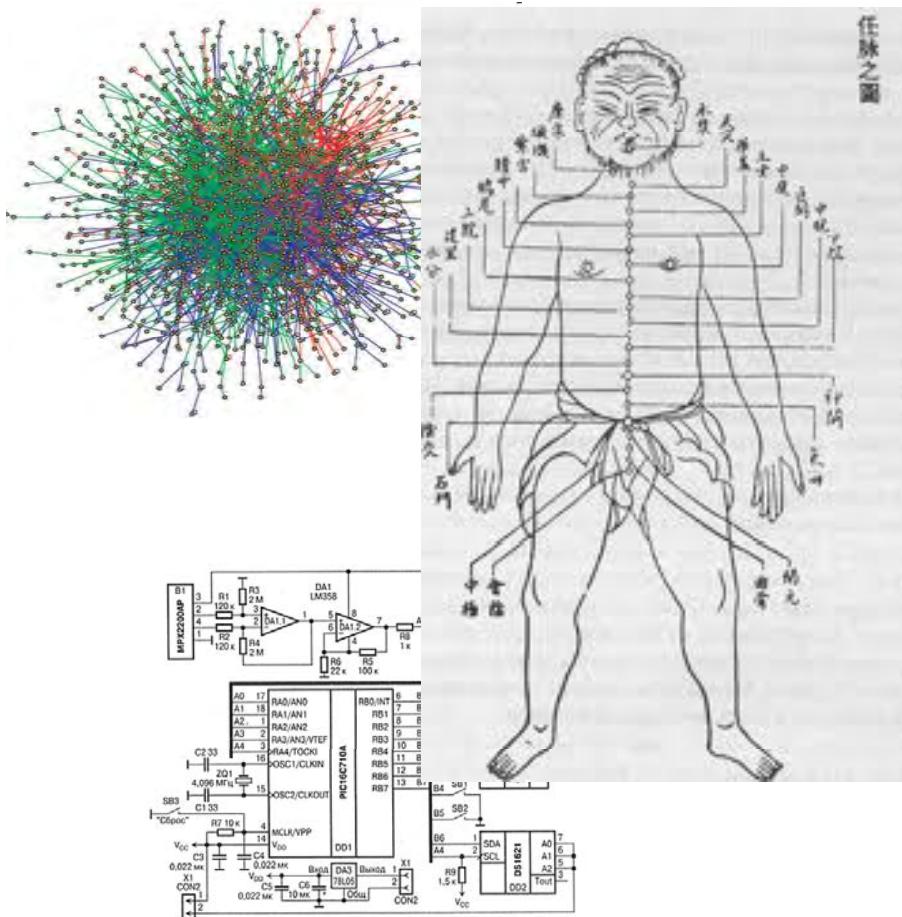
geneXplain



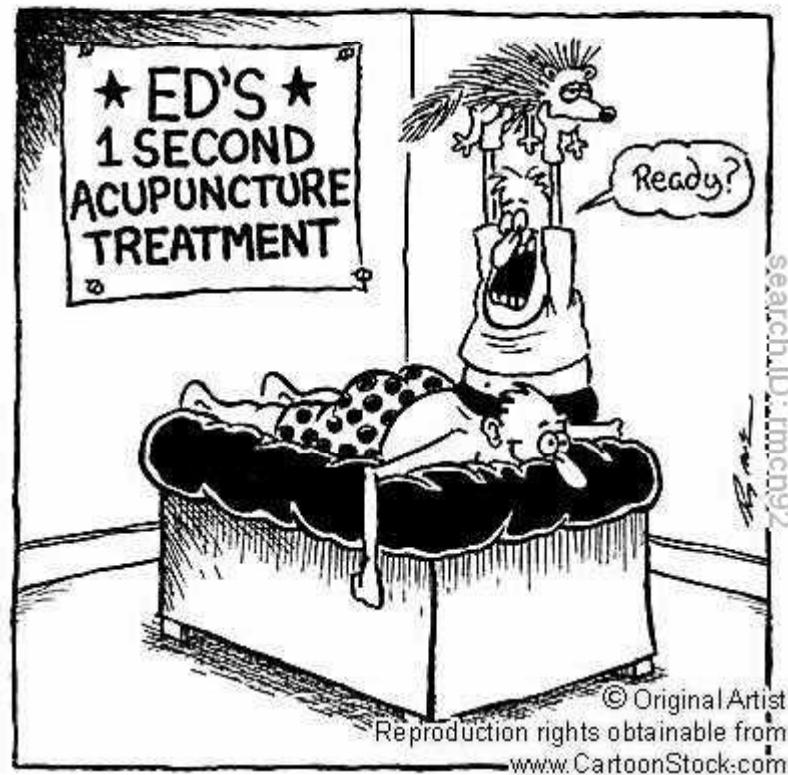
0100100010011101

Institute of Systems Biology

Systems Biology

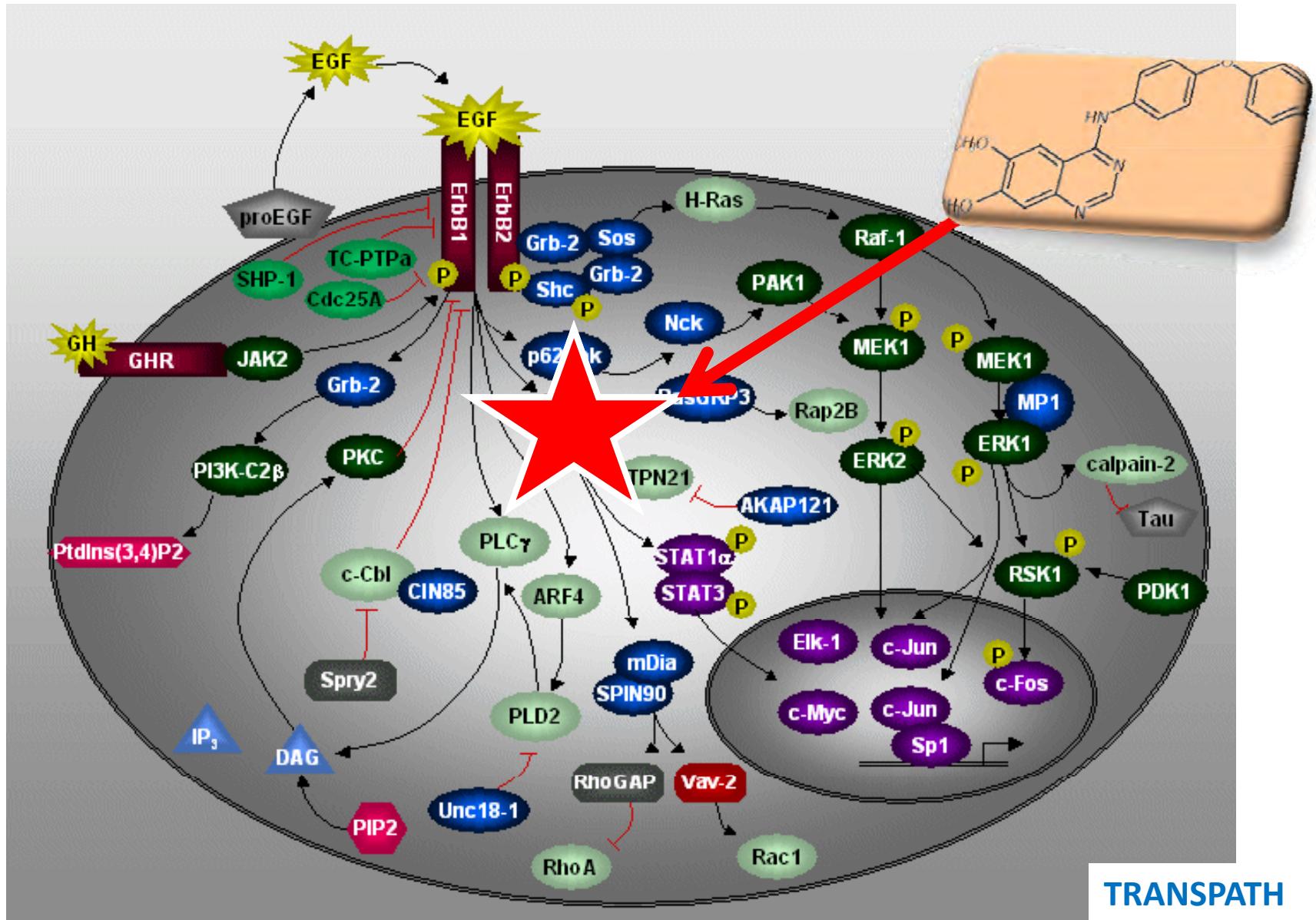


Systems Medicine

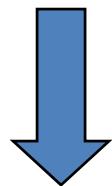
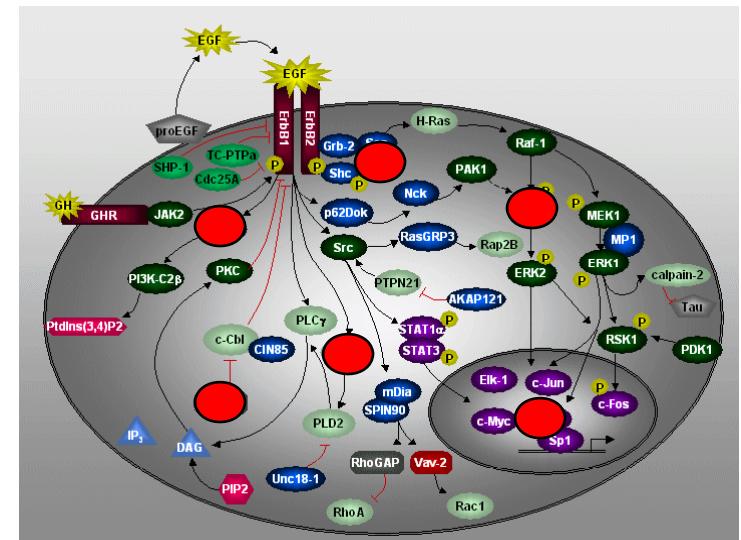
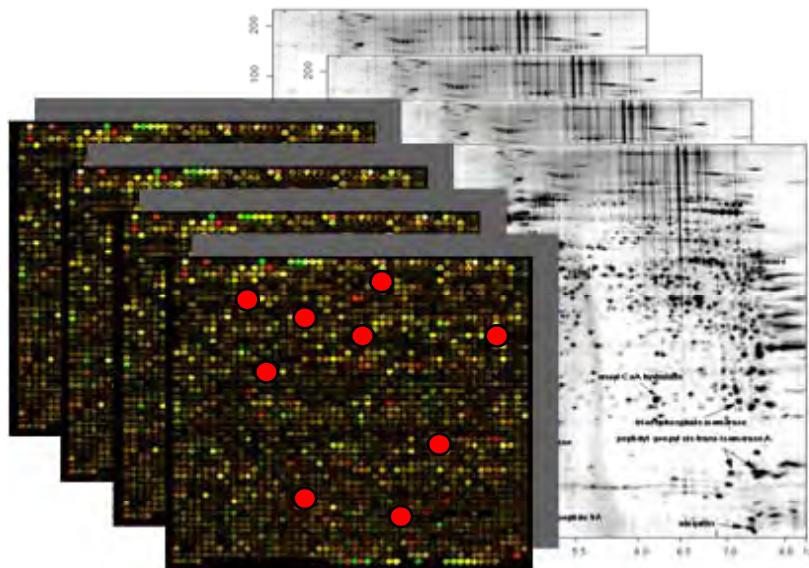


search.ID: rmcn92

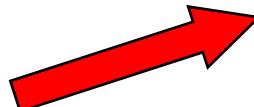
We should find a key pathway of a disease, select a good target and inhibit it.



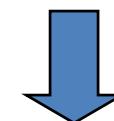
Pathway mapping



Differentially expressed
genes/proteins



Mapping on pathways



Cause of disease ??

Transcriptional profiling of IKK2/NF- κ B– and p38 MAP kinase–dependent gene expression in TNF- α –stimulated primary human endothelial cells

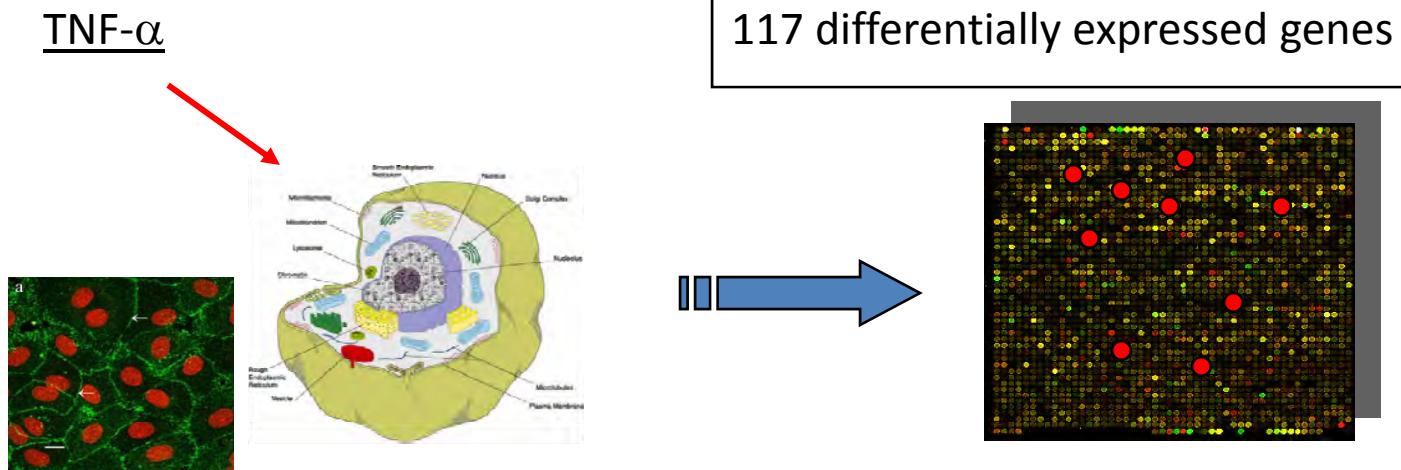
Dorothee Viemann, Matthias Goebeler, Sybille Schmid, Kerstin Klimmek, Clemens Sorg, Stephan Ludwig, and Johannes Roth

Inflammatory stimulation of endothelial cells by tumor necrosis factor α (TNF- α) involves activation of nuclear factor κ B (NF- κ B) and p38 mitogen-activated protein (MAP) kinase signaling pathways. A reliable analysis of the gene expression program elicited by TNF- α and its assignment to distinct signaling pathways is not available. A sophisticated analysis of oligonucleotide microarrays covering more

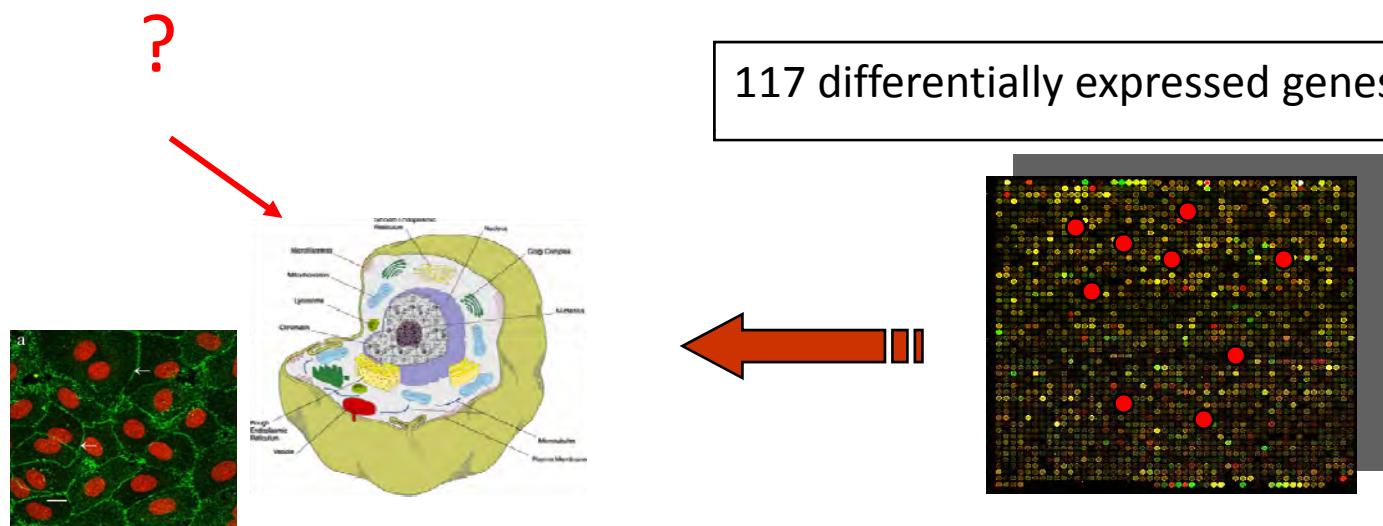
than 13 000 genes allowed definition of the TNF- α –regulated endothelial gene expression profile and novel TNF- α –induced genes. Virtually all TNF- α –inducible genes were dependent on I κ B kinase 2 (IKK2)/NF- κ B activation, whereas a minor number was additionally modulated by p38. Furthermore, genes suppressed by IKK2/NF- κ B were newly identified. Real-time reverse transcriptase–polymer-

ase chain reaction (RT-PCR) and flow cytometry confirmed reliability of data. Thus, these results define a list of primary candidates for targeted modulation of endothelial functions during inflammation. (Blood. 2004;103:3365-3373)

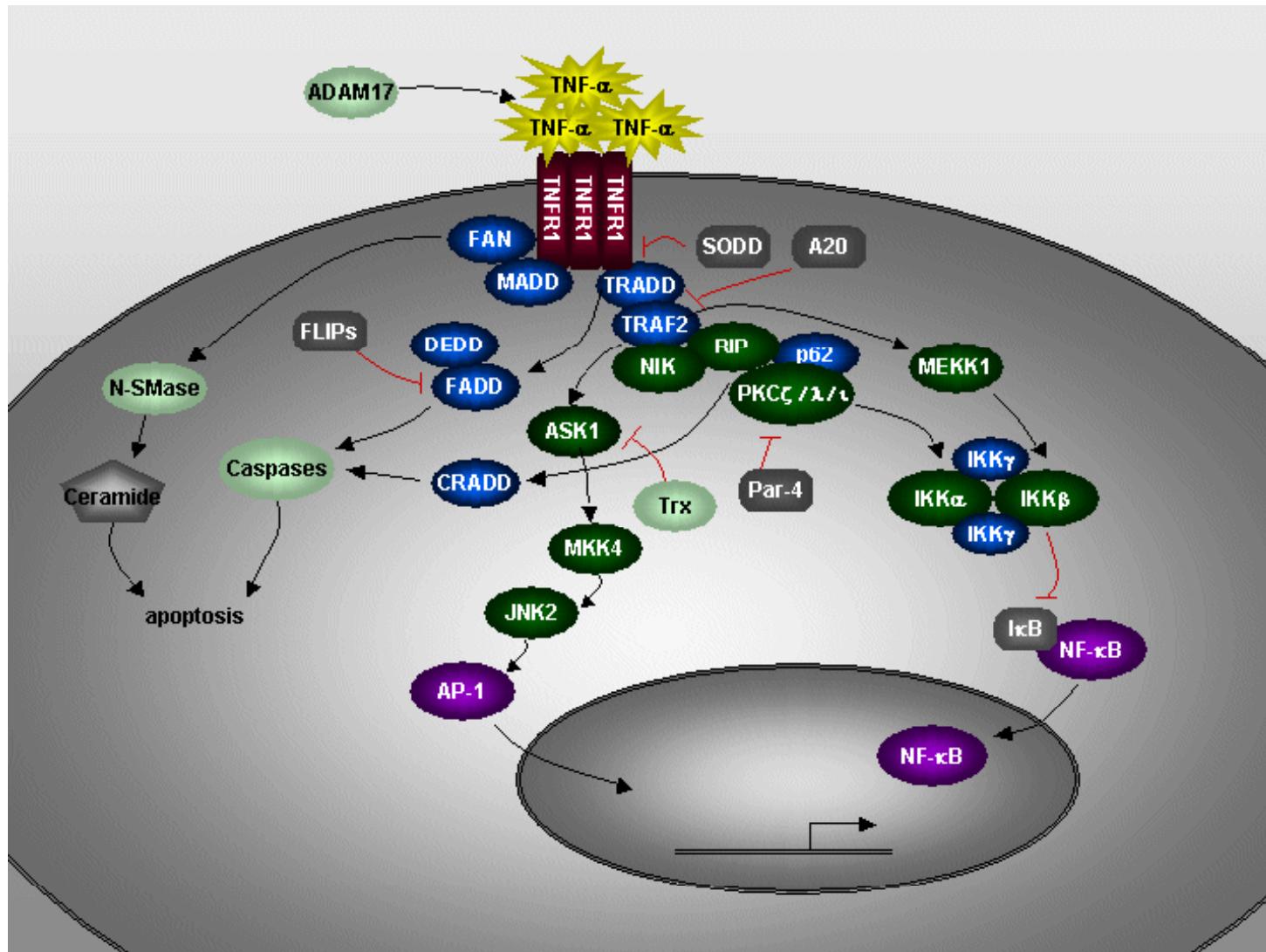
© 2004 by The American Society of Hematology



Can we predict TNF pathway?



Canonical TNF pathway



TRANSPATH

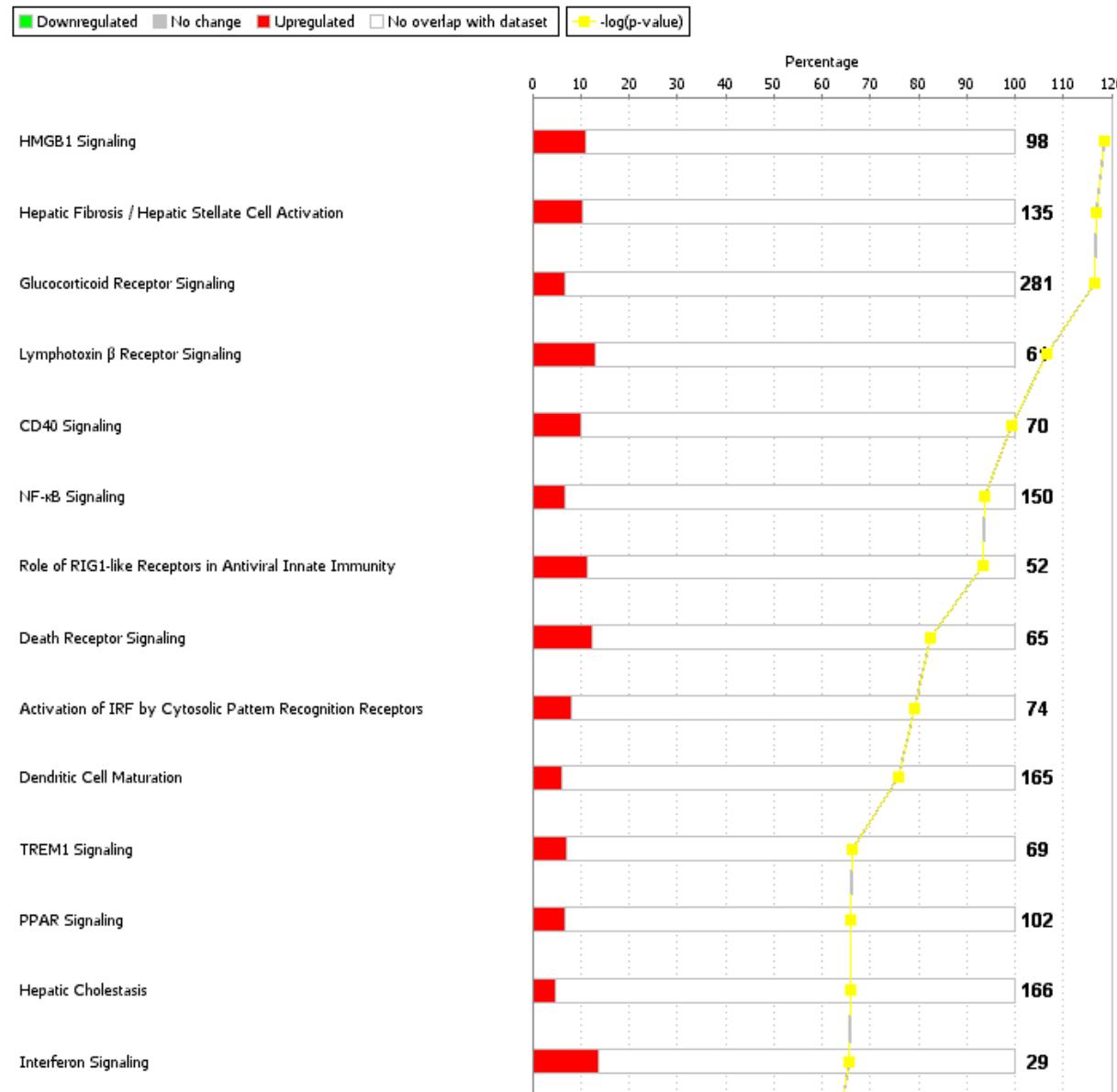
Lets do mapping the differentially expressed genes on canonical pathways.

Pathway name	Hits	Pathway_id	Hit names	Pathway size	p-value
M-CSF ---> c-Ets-2	2	CH000000060	ETS2; CSF1	5	3.07E-03
IFNalpha, IFNbeta, IFNgamma ---> Rap1	3	CH000000595	IFNGR1; TYK2; IFNGR2	19	4.34E-03
Epo ---Lyn---> STAT5A	2	CH000000524	STAT5A; LYN	6	4.56E-03
activin A ---> Smad3	2	CH000000680	INHBA; SMAD3	10	1.31E-02
IFN pathway	3	CH000000740	IFNGR1; TYK2; IFNGR2	29	1.44E-02
Sonic Hedgehog pathway	2	CH000001022	MTSS1; PTCH	19	4.48E-02
hypoxia pathways	2	CH000000987	CDKN1B; NRIP1	21	5.38E-02
EDAR pathway	2	CH000000759	NFKBIA; CYLD	27	8.40E-02
Epo pathway	2	CH000000741	STAT5A; LYN	32	1.12E-01
TGFbeta pathway	3	CH000000711	BMP2; INHBA; SMAD3	72	1.39E-01
IL-22 pathway	1	CH000000762	TYK2	9	1.51E-01
IL-10 pathway	1	CH000000761	TYK2	9	1.51E-01
VEGF-A pathway	2	CH000000723	NOS3; VEGFA	42	1.75E-01
TLR3 pathway	2	CH000000820	TANK; IKBKE	44	1.88E-01
IL-8 pathway	2	CH000000786	CXCL1; IL8	46	2.01E-01
TNF-alpha pathway	2	CH000000772	NFKBIA; OSIL	53	2.48E-01
p38 pathway	2	CH000000849	MAP2K3; DUSP8	55	2.61E-01

Not significant

TNF pathway can not be found by direct maping on canonical pathways....

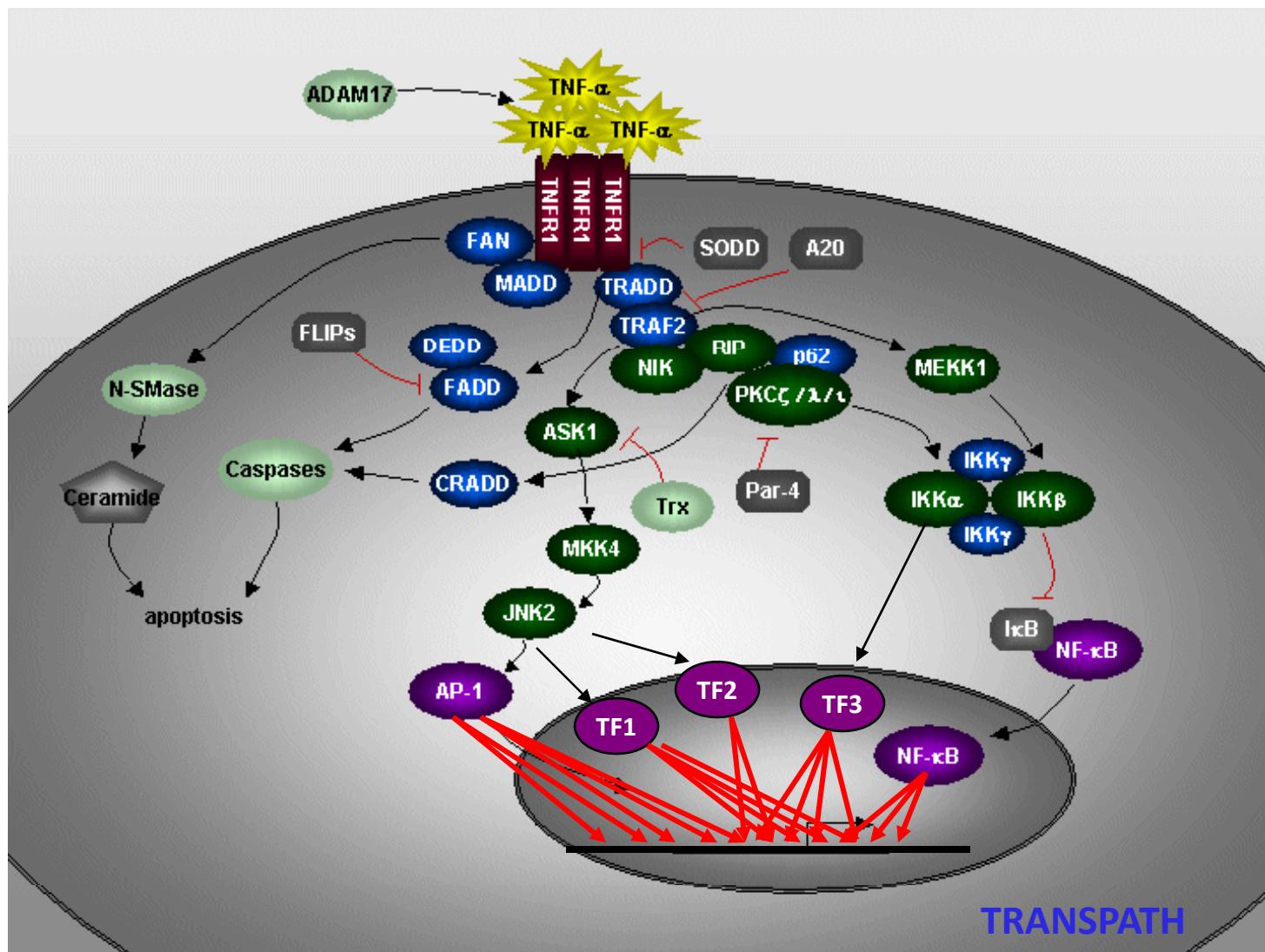
Mapping on canonical pathways (using Ingenuity)



**Mapping on pathways does
not work
(even in such a simple case)**

Why ?

***BIG gap of knowledge on
interactions between TF and their target sites in DNA***



Enhanceosome

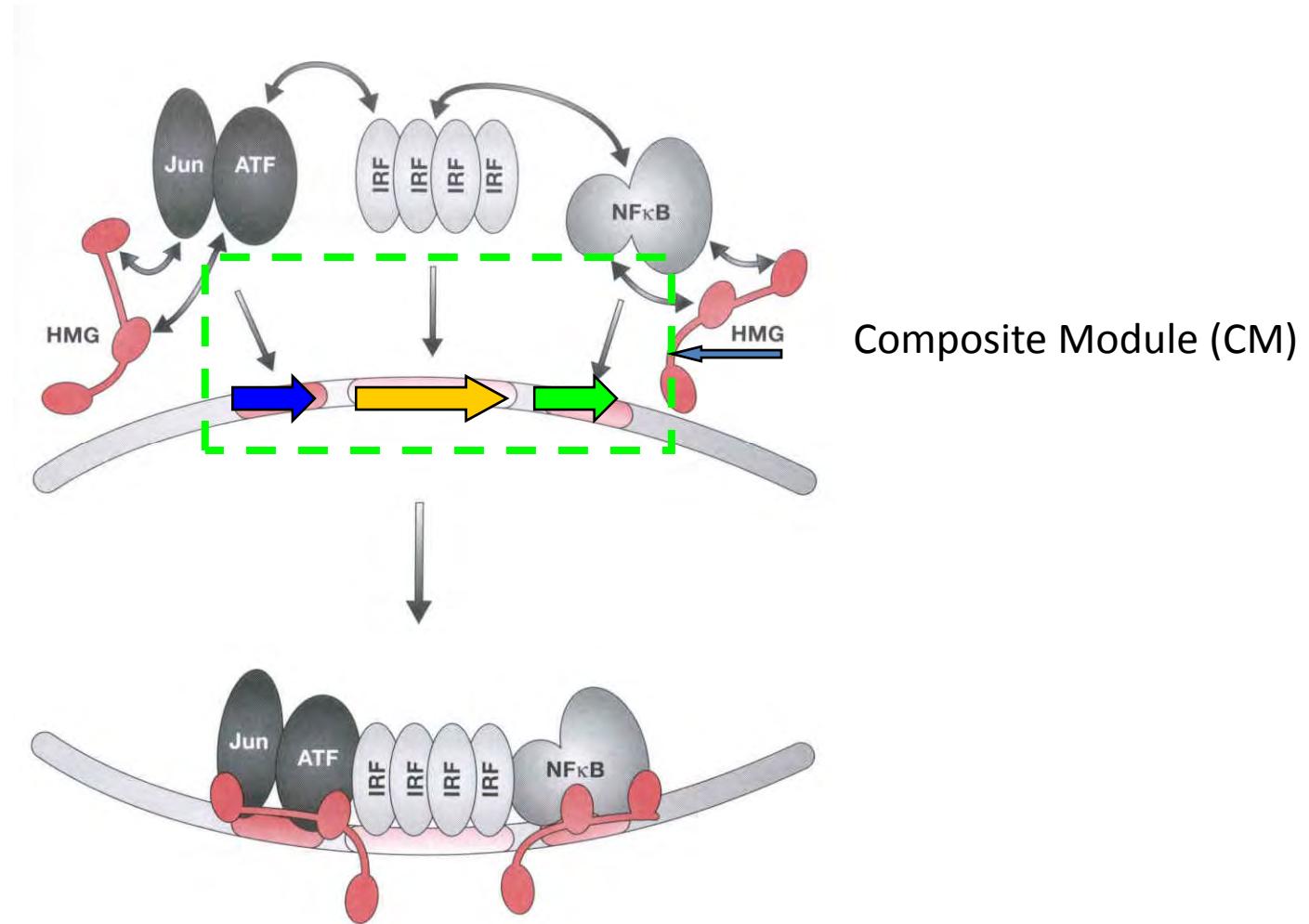
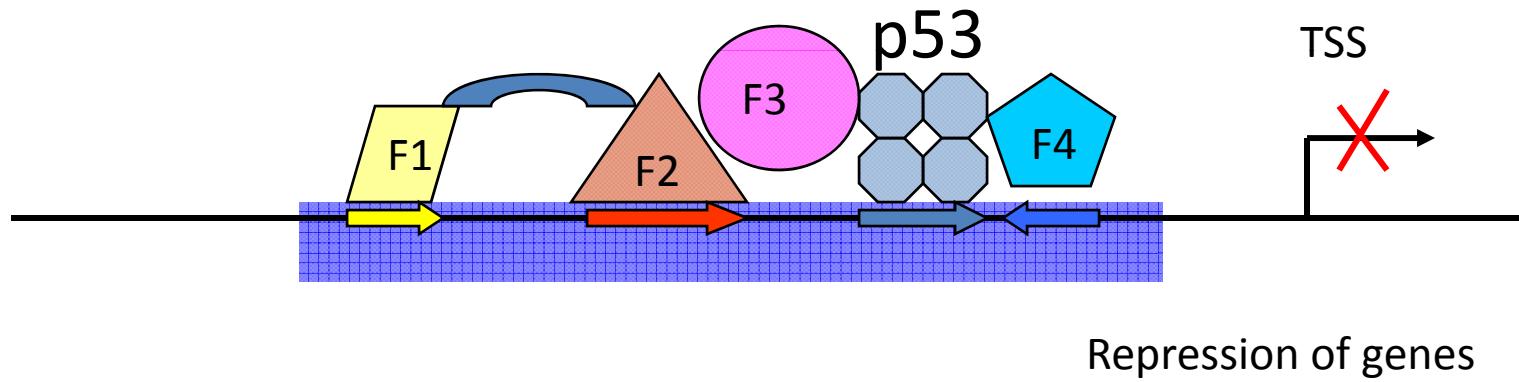
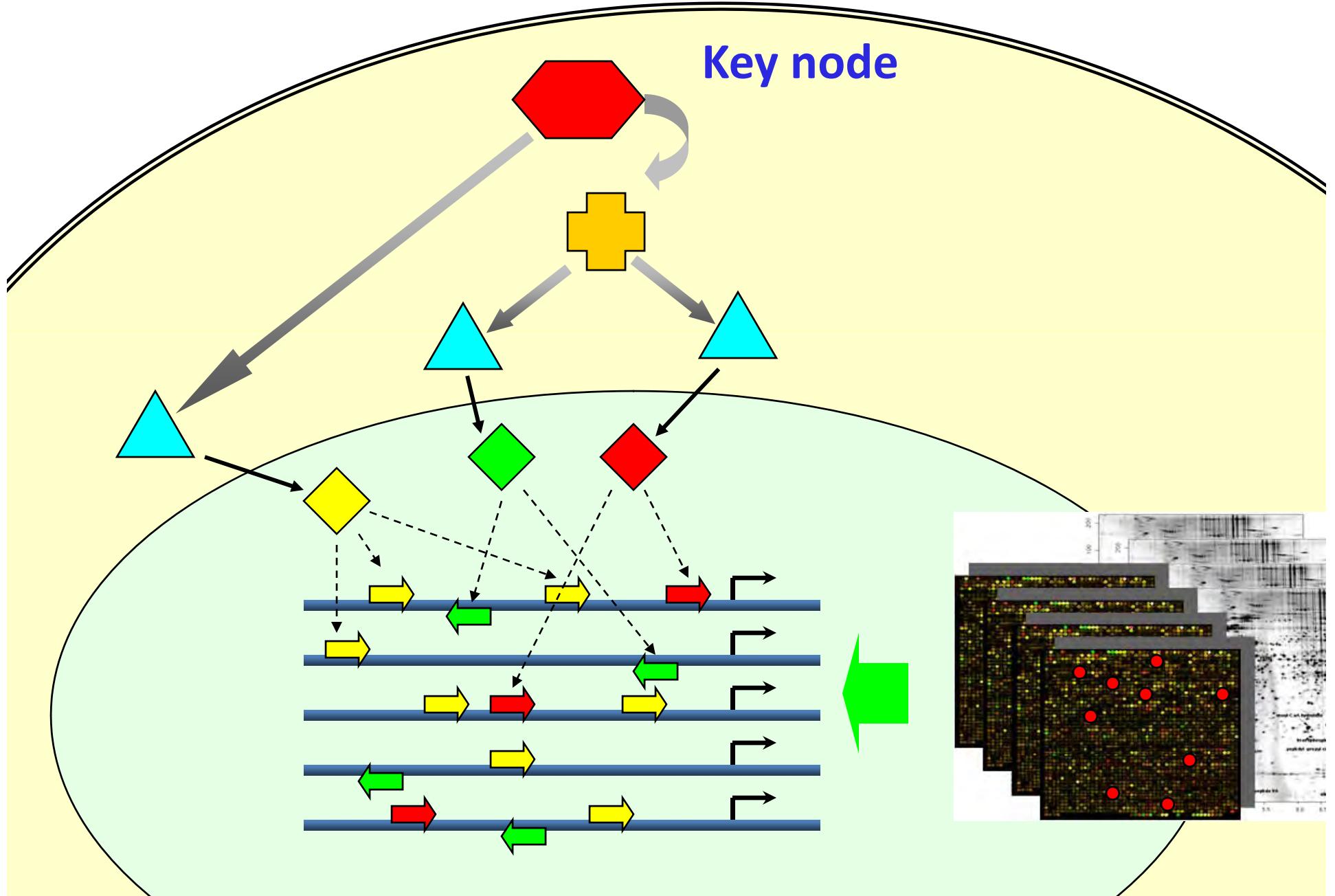


FIGURE 3.3. The human interferon- β enhanceosome. HMG represents HMGI/Y, a ubiquitous protein that binds cooperatively with the three activators. HMGI/Y both bends the DNA and contacts the activators. Each of the transcription factors shown is a member of a family of related activators. (Mark Ptashne, Alexander Gann Genes and Signals, 2002)

Enhanceosome binding aria



Key node



BiML /geneXplain platform – target discovery pipeline

The screenshot displays the BiML /geneXplain platform interface, featuring several windows and panels:

- Top Left Panel:** Shows a tree view of analyses, including "GSM409563.txt.txt", "GSM409564.txt.txt", "GSM409565.txt.txt", "GSM409566.txt.txt", "GSM409567.txt.txt", "GSM409568.txt.txt", and "GSM409569.txt.txt".
- Top Right Panel:** A table titled "Analyses" with columns: ID, name, title, and SURE-p-value. The table lists 136 rows of data, with the first few rows shown below:

ID	name	title	SURE-p-value
A_32_P5889	ENSG00000111052	LIN7A	-93.26158912
A_24_P55145	ENSG00000140015	KCNH5	-63.50408857
A_23_P50053	ENSG00000107796	ACTA2	-65.69025229
A_24_P43810	ENSG00000147629	FAM13A	-55.39815975
A_25_P5362	ENSG00000152328	TP300	-57.36568093
A_32_P40361	ENSG00000196576	PLXNB2	-55.18324829
A_24_P88526	ENSG00000214725	AC120114.2	-54.62388943
A_23_P82719	ENSG00000163888	LIPK	-53.39217457
A_23_P52986	ENSG00000245792	VWC2	-53.62089509
A_24_P70588	ENSG00000196576	PLXNB2	-53.10527399
- Top Center Panel:** A "Convert table" window showing a table with columns: ID, name, title, and SURE-p-value.
- Middle Left Panel:** A network diagram showing interactions between genes like E2F1, pRb, and pRbip. Below it is a "Termination result" graph showing "Quantity or Concentration" over "Time" for various molecules, with curves for E2F1, Cyclin D1, pRb, pRbip, and others.
- Middle Right Panel:** A flowchart illustrating the target discovery pipeline:


```

graph TD
    A[Gene sites on gene set] --> B[Sites]
    B --> C[summary]
    C --> D[Matrices to molecules]
    D --> E[Molecules]
    E --> F[Regulator search]
    F --> G[Gene set Transpath]
    G --> H[Convert table(2)]
    H --> I[Sites]
    I --> A
    
```
- Bottom Panel:** A hierarchical tree diagram showing relationships between various entities.
- Description:**

In this analysis, gene expression was compared between lesion skin and uninvolved skin of the same 28 patients. The following were the steps of analysis shown here.

 1. CEL file normalization. This step resulted in two files, Experiment normalized (MAS5) and Control normalized (MAS5).

07/09/2011

Master regulator search results of TNF-alpha regulated transcription.

Screenshot of a bioinformatics software interface showing search results for TNF-alpha regulated transcription.

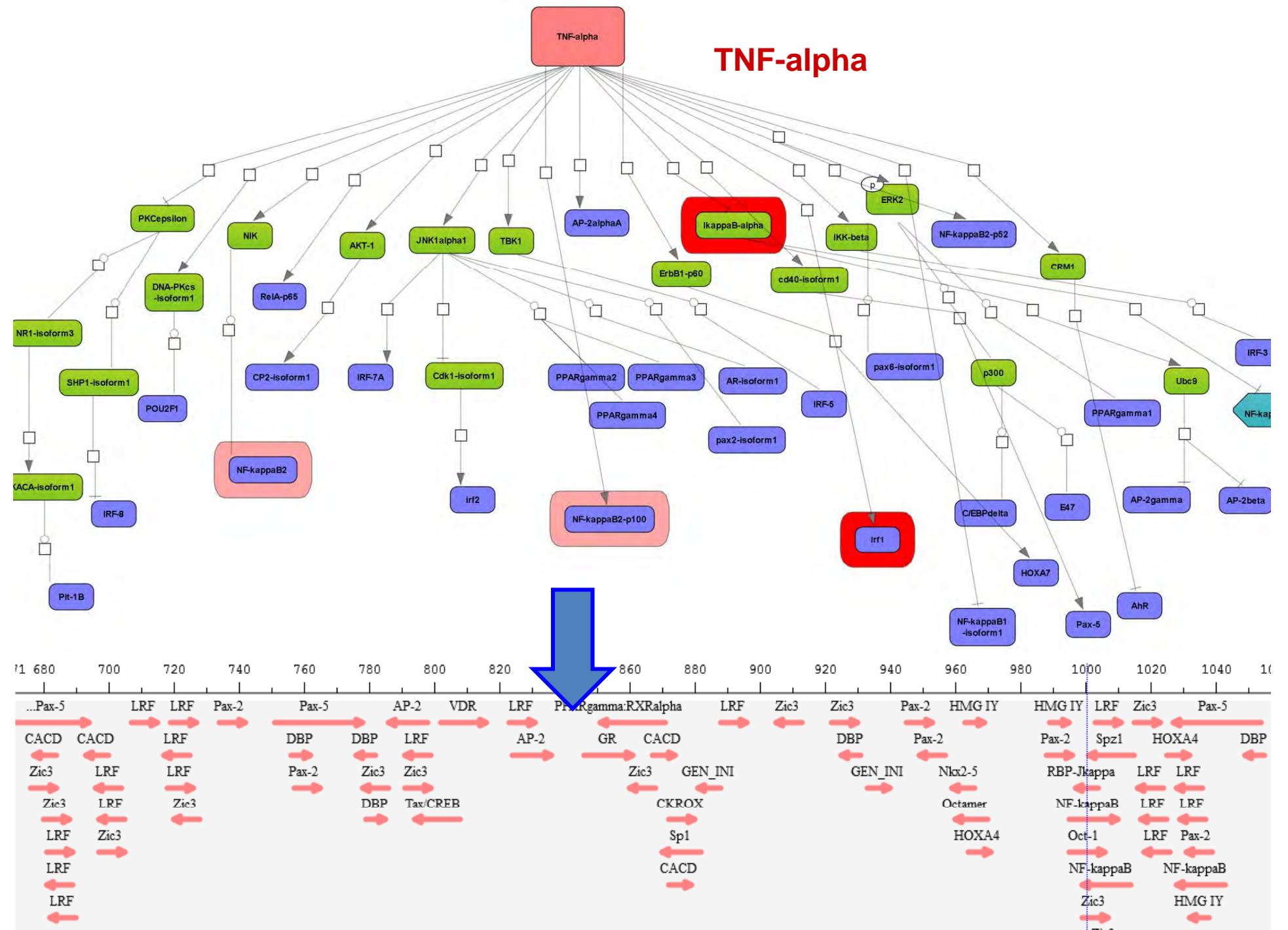
The main window displays a table of 4263 entries, showing the following columns:

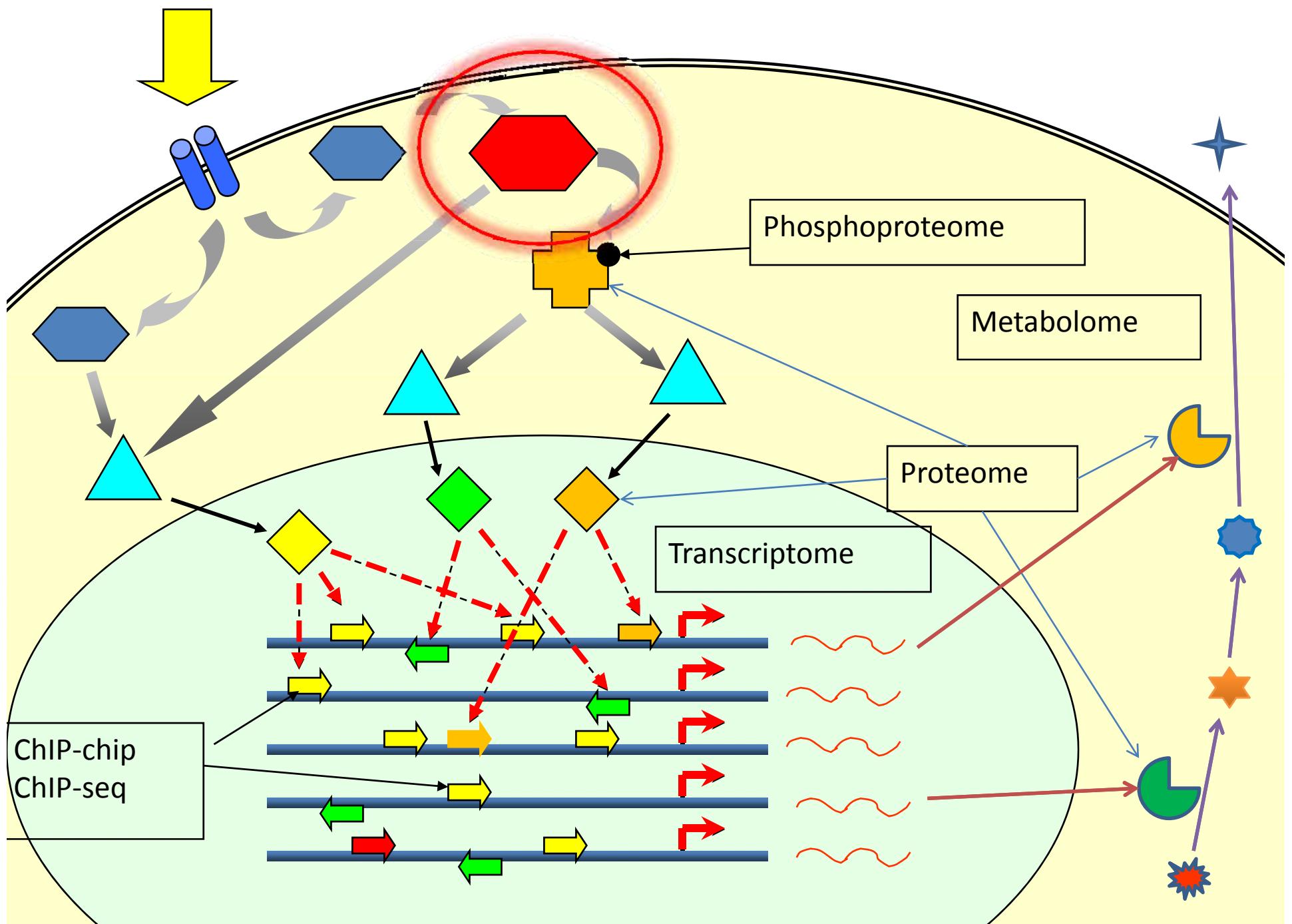
- ID
- Master molecule name
- Reached from set
- Reachable total
- Score

The table lists various molecules, with several entries circled in red:

ID	Master molecule name	Reached from set	Reachable total	Score
MO000081833	JNK1alpha2(h)	35	26650	0.8978
MO000081834	JNK1beta2(h)	35	26650	0.8978
MO000033485	JNK1beta1(h)	35	26650	0.89778
MO000030998	JNK1alpha1(h)	35	26650	0.89778
MO000058481	AKT-1(h)	36	26202	0.85334
MO000060489	TNF-alpha(h)	35	25969	0.7198
MO000056837	ERK2(h)	36	25836	0.71737
MO000034342	ERK2(II)(P)	35	24912	0.6738
MO000056883	ERK1(h)	35	25807	0.65982
MO000058803	PDK1-isoform1(h)	35	25342	0.64517
MO000059481	PKCepsilon(h)	35	25314	0.64188
MO000019985	p300(h)	36	23451	0.61833
MO000020398	Caspase-3(h)	35	24877	0.61621
MO000141330	MKP-2(h)	33	25143	0.6118
MO000059863	CSBP1(h)	35	25033	0.6066
MO000059867	CSBP2(h)	35	25033	0.6066
MO000059869	EXIP(h)	35	25033	0.6066
MO000085411	Mxi2(h)	35	25033	0.6066
MO000057624	PKCalpha(h)	35	25387	0.60411
MO000100964	AKT-2(h)	33	24744	0.60349
MO000105854	Caspase-3(h)	35	25009	0.59625
MO000059577	PKCdelta(h)	35	25021	0.59488
MO000122463	mTOR(h):rictor(h):mLST8(h):SIN1(h)	34	24920	0.59215
MO000099197	ILK(h)	34	24972	0.59168
MO000041374	MKK4beta(h)	34	25140	0.59086
MO000083769	MKP-1(h)	33	24863	0.58487

The sidebar on the left shows a tree view of databases and analyses, with the "Molecules2 Upstream 8" node expanded. The bottom status bar indicates the ID is Molecules2 Upstream 8, the size is 4263, and the complete name is data/Projects/iamado@itnb.unl.edu/Data/TNF_Genes_Eensembl.





Main topics

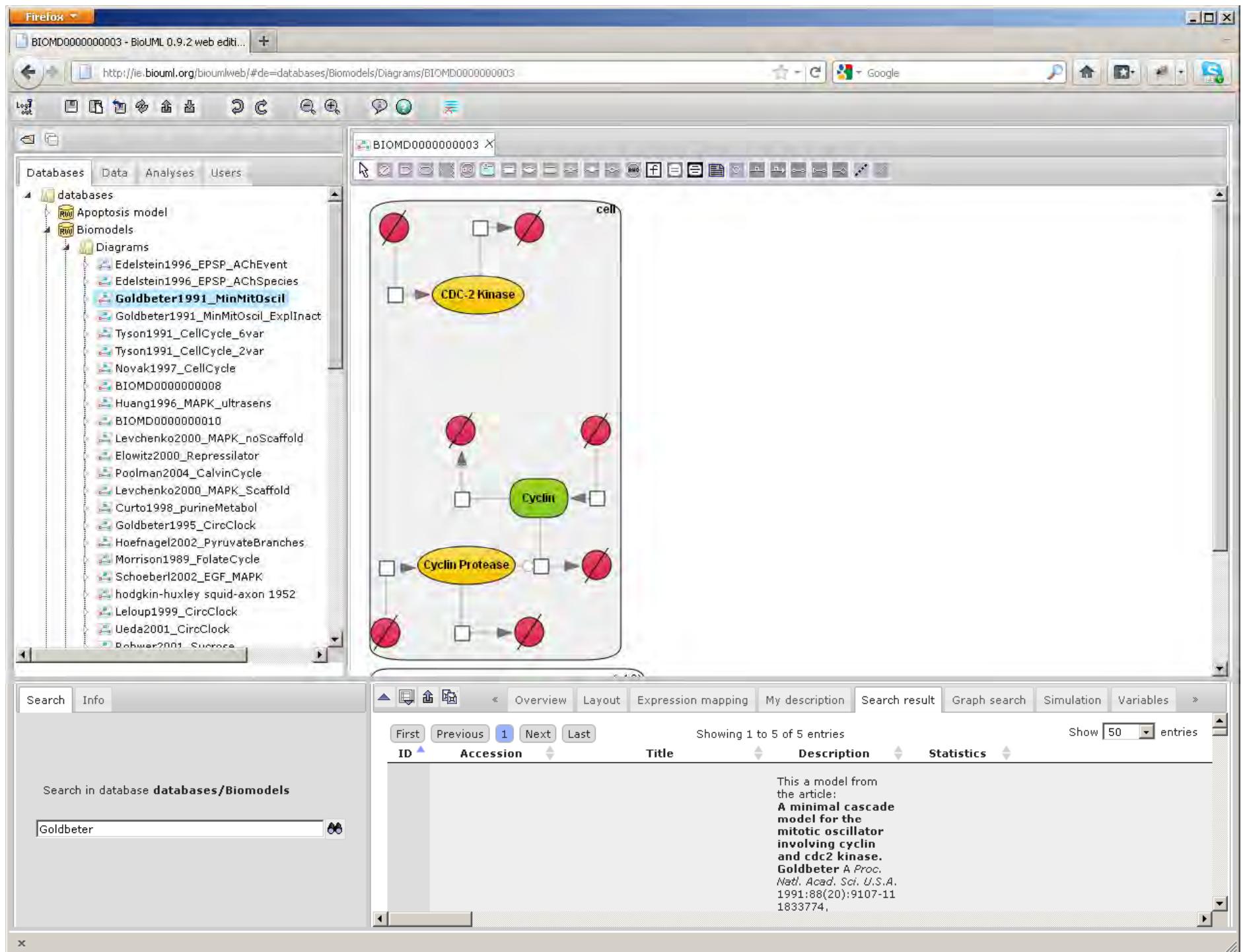
- supported standards: SBML, SBGN, BioPAX, SED-ML, SBO, MIRIAM, CellML
 - some examples, CellDesigner extension support
 - state concept
 - SED-ML as workflow
 - internal world of BioUML for these formats support (meta-model)
- Modular modelling: composite models, agent based models
- systems biology – reproducible hightthroughput data analyses:
 - analyses: algorithms, scripts, workflows
 - integration with R/Bioconductor, Galaxy
 - data: microarrays, NGS, ChIP-SEQ
 - visualization: genome browser
- BioUML – as platform for collaborative research
 - Amazon EC2 servers
 - data repository - groups, projects, import/export, FTP upload
 - chat, history
- current works: Biostore, LIMS (laboratory information management system)

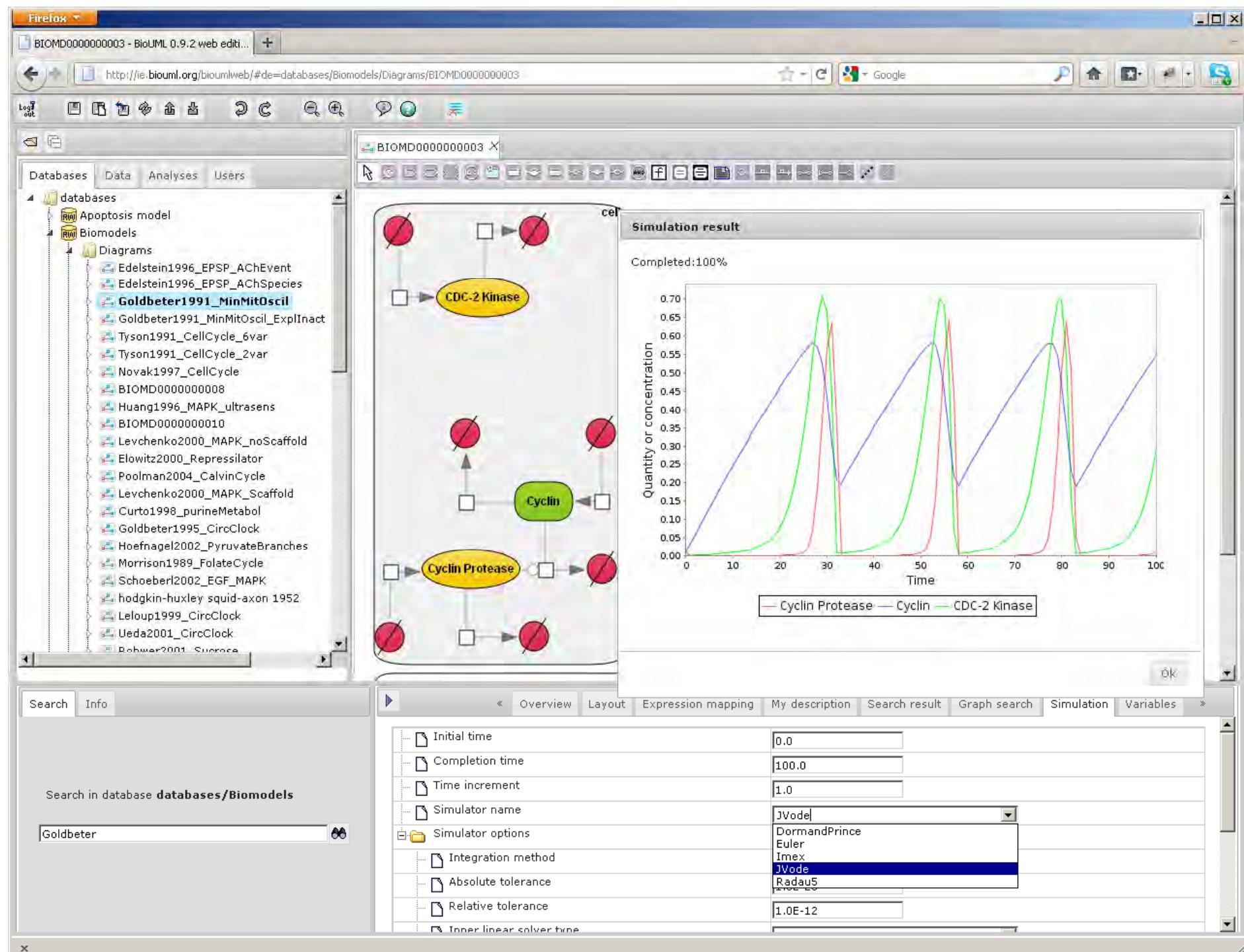
Standard supports:

SBML, SBGN, BioPAX, SED-ML, SBO,
MIRIAM, CellML

SBML support

- import/export - level 1, 2, 3 (core)
- passed all tests from SBML test suite version 2.0.0 beta 1
(2010, April 2)
- extensions:
 - CellDesigner
 - SBGN-PD (own XML format)
- Biomodels
 - full text search
 - SBGN -PD (parse RDF annotation do determine specie types)
 - layout algorithms
 - on-line simulation
- Panther DB
 - full text search
 - reads CellDesigner extensions
 - SBGN-PD





Firefox - BIOMD0000000003 - BioML 0.9.2 web editor

http://ie.bioml.org/biomlweb/#de=databases/Biomodels/Diagrams/BIOMD0000000003

Log out Databases Data Analyses Users

databases

- Apoptosis model
- Biomodels
- Diagrams
 - Edelstein1996_EPSP_AChEvent
 - Edelstein1996_EPSP_AChSpecies
 - Goldbeter1991_MinMitOscil**
 - Goldbeter1991_MinMitOscil_ExplInact
 - Tyson1991_CellCycle_6var
 - Tyson1991_CellCycle_2var
 - Novak1997_CellCycle
 - BIOMD0000000008
 - Huang1996_MAPK_ultrasens
 - BIOMD0000000010
 - Levchenko2000_MAPK_noScaffold
 - Elowitz2000_Repressilator
 - Poolman2004_CalvinCycle
 - Levchenko2000_MAPK_Scaffold
 - Curto1998_purineMetabol
 - Goldbeter1995_CircClock
 - Hoefnagel2002_PyruvateBranches
 - Morrison1989_FolateCycle
 - Schoeberl2002_EGF_MAPK
 - hodgkin-huxley squid-axon 1952

BIOMD0000000003 X

V3 = "\$cell.M" * VM3
V1 = "\$cell.C" * VM1 * ("\$cell.C"+Kc)^{-1.0}

The diagram illustrates a compartmentalized model of cell cycle regulation. It features three main compartments represented by green and yellow ovals: 'Cyclin' (green), 'Cyclin Protease' (yellow), and 'CDC-2 Kinase' (yellow). Each compartment contains a red circular node representing a protein. Arrows indicate interactions between these nodes and the compartment boundaries, representing transport or feedback loops. The 'Cyclin' compartment has two outgoing arrows to the 'Cyclin Protease' and 'CDC-2 Kinase' compartments. The 'Cyclin Protease' compartment has one outgoing arrow to the 'CDC-2 Kinase' compartment. The 'CDC-2 Kinase' compartment has one outgoing arrow back to the 'Cyclin' compartment.

Search **Info**

Search in database **databases/Biomodels**

Goldbeter

Layouter: Cross cost grid layout (with compartments)

- Grid
- Grid
- Cross cost grid layout (with compartments)
- Num
- Cooling coefficient
- Perturbation threshold
- Max distance

Variables

$V1 = \$cell.C * VM1 * (\$cell.C + Kc)^{-1.0}$
 $V3 = \$cell.M * VM3$

Firefox - Biotin_biosynthesis - BioUML 0.9.2 web edition

http://ie.biouml.org/bioumlweb/#de=databases/PantherDB/Diagrams/Biotin_biosynthesis

Databases Data Analyses Users

Biotin_biosynthesis X

Databases

- Apoptosis model
- Biomodels
- Biopath
- EHMN
- Ensembl
- GO
- PASS
- PantherDB
- Diagrams

 - 2-arachidonylglycerol_biosynthesis
 - 5-Hydroxytryptamine_biosynthesis
 - 5-Hydroxytryptamine_degradation
 - 5HT1_type_receptor-mediated_signaling
 - 5HT2_type_receptor-mediated_signaling
 - 5HT3_type_receptor-mediated_signaling
 - 5HT4_type_receptor-mediated_signaling
 - ATP_synthesis
 - Acetate_utilization
 - Adenine_and_hypoxanthine_salvage_p
 - Adrenaline_synthesis
 - Alanine_biosynthesis
 - Allantoin_degradation
 - Alpha_adrenergic_receptor_signaling

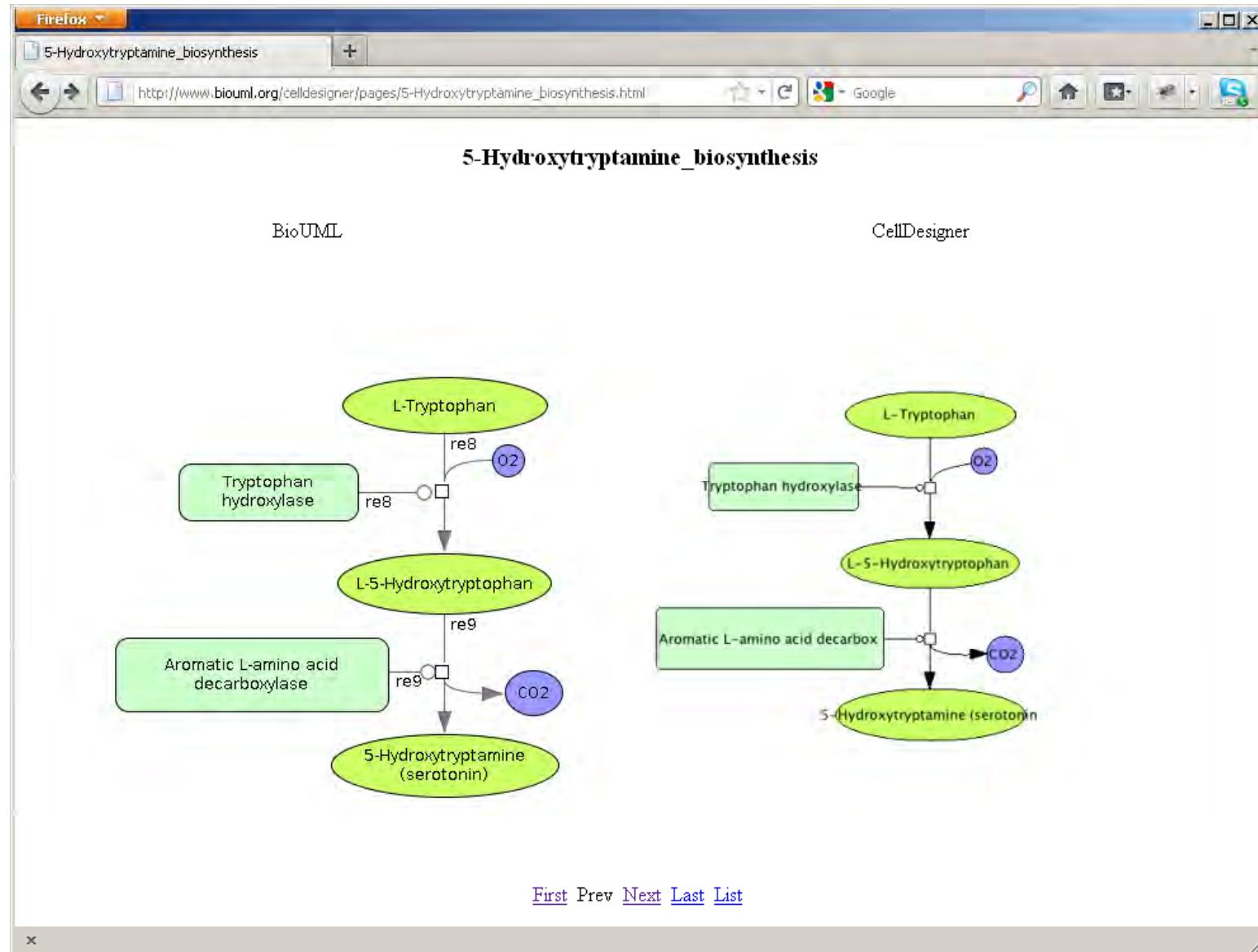
Search | Info

Search in database databases/PantherDB

Search result

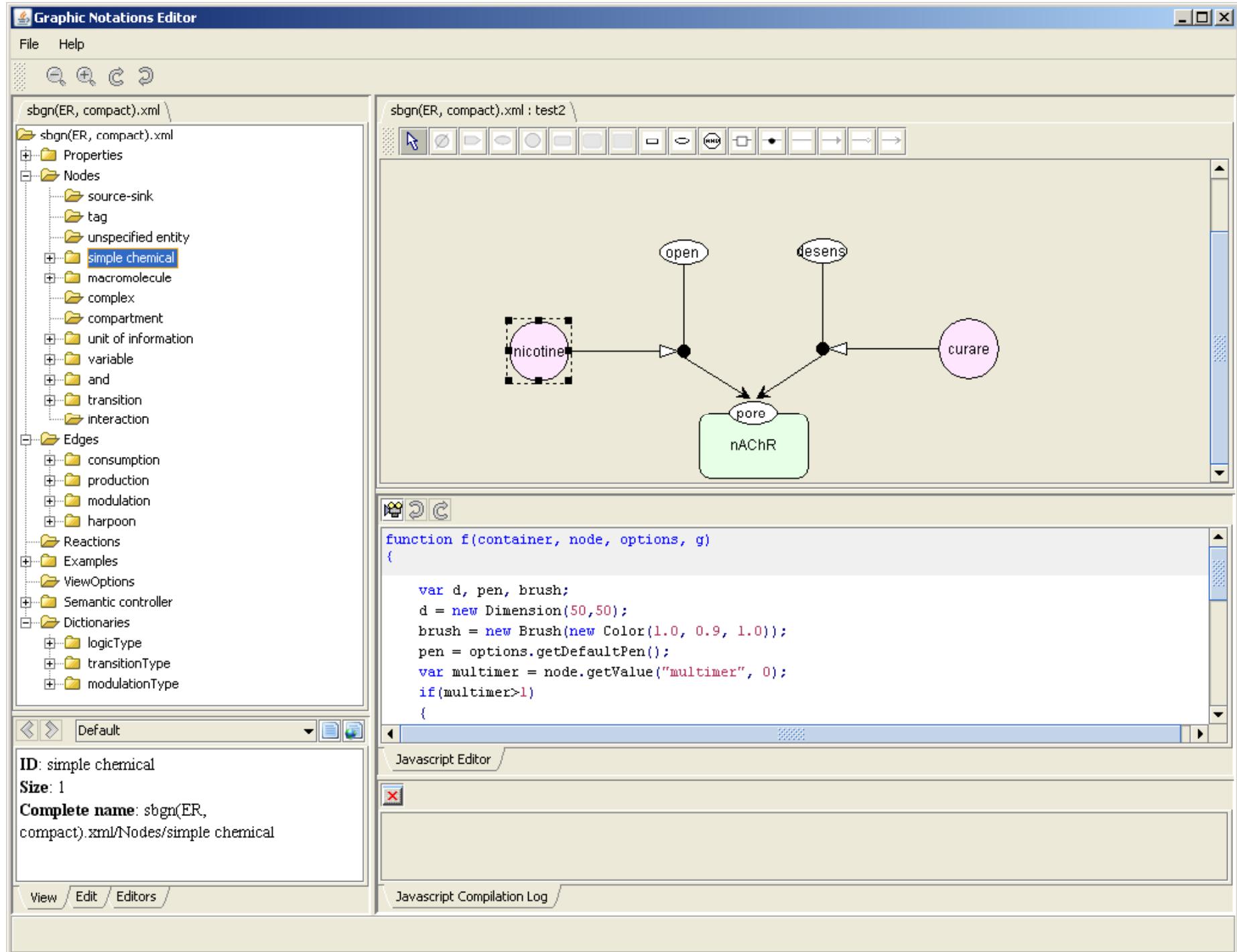
ID	Accession	Title	Description	Statistics	Components
0	Biotin_biosynthesis	Biotin_biosynthesis	Biotin is an essential enzyme ...	components:20, reactions:4, ed...	default, s1, s10, s11, s12, s13, s14, s15, s16, s17, s18

CellDesigner support – comparison for 165 images from Panther DB and generated by BioUML



SBGN support

- diagram types: PD – beta; ER, AF – alpha
- defined as XML graphic notation for BioUML
- graphic notation can be edited using BioUML graphic notation editor
- special extension for SBML
- Reactome - SBGN-PD
 - full text search
 - SQL version is used
 - read diagram layout from Reactome
- BioPAX – SBGN-PD
 - level 2 (beta), level 3 (alpha)
 - auto layout
- TRANSPATH – SBGN-PD
 - full text search
 - auto-layout



Reactome

http://ie.biouml.org/bioumlweb/#de=databases/Reactome/Diagrams/662639

Log out Research test

Databases Data Analyses Users

PantherDB Reactome

Data

Diagrams

- ABC-family proteins mediated transport
- Advanced glycosylation end products
- APC/C-mediated degradation
- Apoptosis
- Apoptotic execution phase
- Aquaporin-mediated transport
- Asparagine N-linked glycosylation
- Axon guidance
- Base Excision Repair
- Bile acid and bile salt metabolism
- Binding of RNA by Insulin-like growth factor II receptor
- Biological oxidations
- Botulinum neurotoxicity
- Cell Cycle Checkpoints
- Cell Cycle, Mitotic
- Cell junction organization
- Cell surface interactions at the plasma membrane
- Cholesterol biosynthesis
- Chromosome Maintenance
- Circadian Clock

JavaScript log X 662639 X

long-chain fatty acids [cytosol]

H₂O [cytosol]

ATP [cytosol]

PEX3 [peroxisomal membrane]

ABCD1/ABCD3 heterodimer [peroxisomal membrane]

ADP [cytosol]

long-chain fatty acids [peroxisomal matrix]

Orthophosphate [cytosol]

Search Info

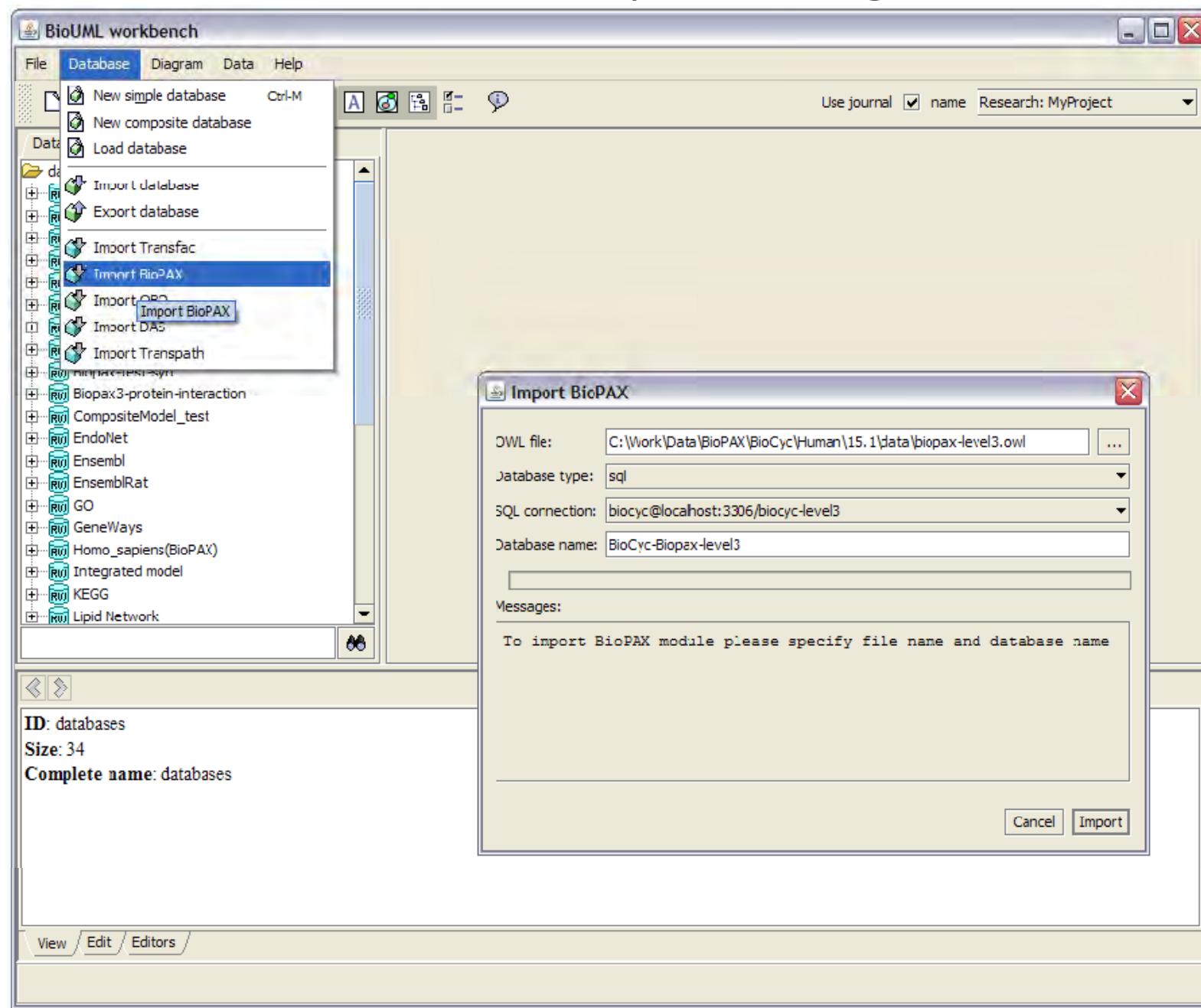
Search in database databases/Reactome

proteins transport

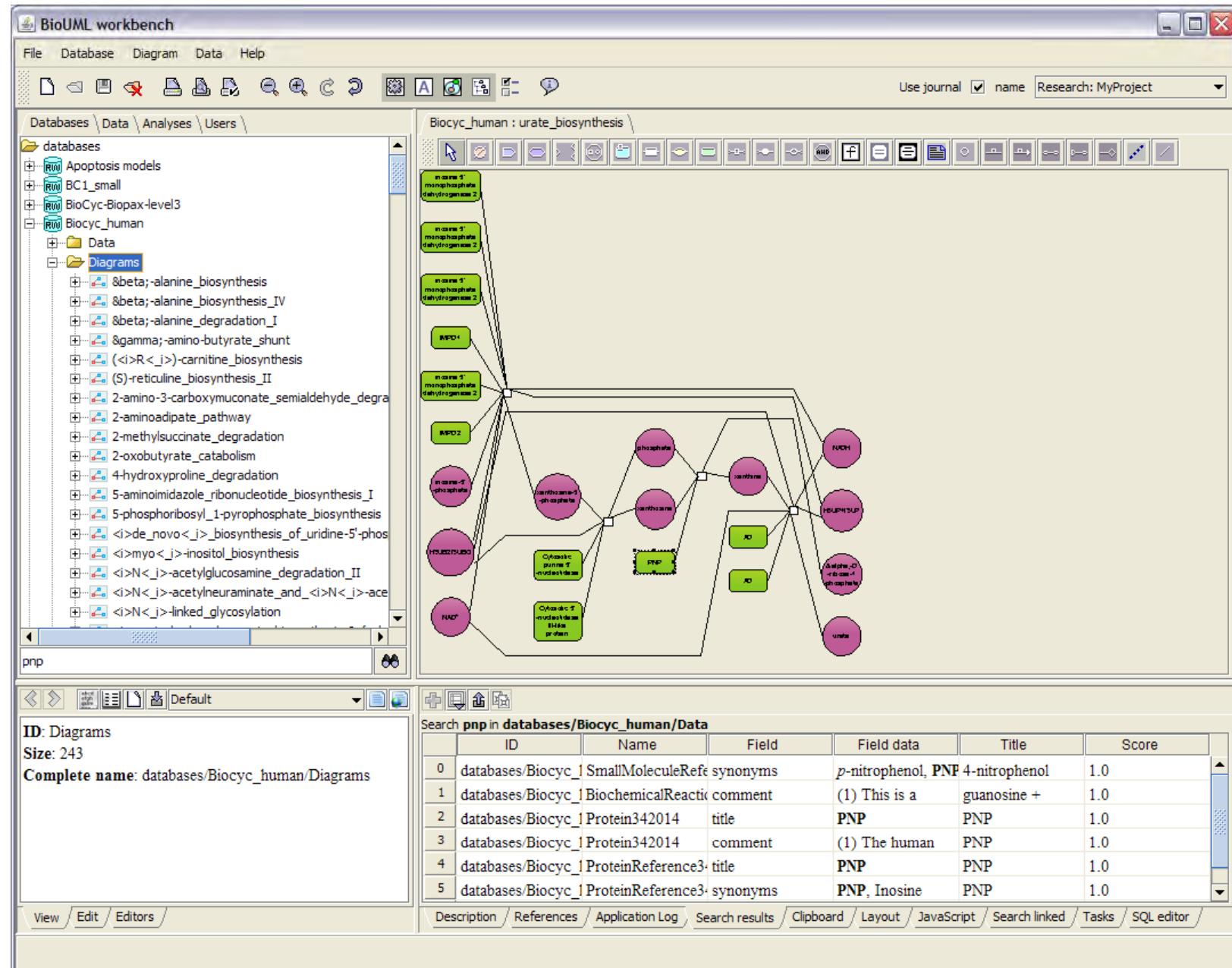
ID Accession Title

ID	Accession	Title
0	662639	ABC-family proteins mediated transport PEX19:ABCD1/ABCD3 [cytosol], CFTR [membrane], long-chain fatty acids [peroxisomal matrix]
1	482784	APC/C-mediated degradation of cell cycle proteins MAD2*CDC20 complex [cytosol], 26S proteasome [cytosol], Cdc20 [cytosol], PLK1 [cytosol]
10	451063	Gap junction trafficking and regulation Cx43:20-1 [Golgi-associated vesicle membrane], c-src-associated Cx43 junctions
11	835437	Gene Expression L-serine [cytosol], CycC [nucleoplasm], MED13 [nucleoplasm], MED25 [nucleoplasm]
12	481014	Hemostasis RACGAP1 [cytosol], PP2A [cytosol], Coxsackievirus and adenovirus receptor [plasma membrane]

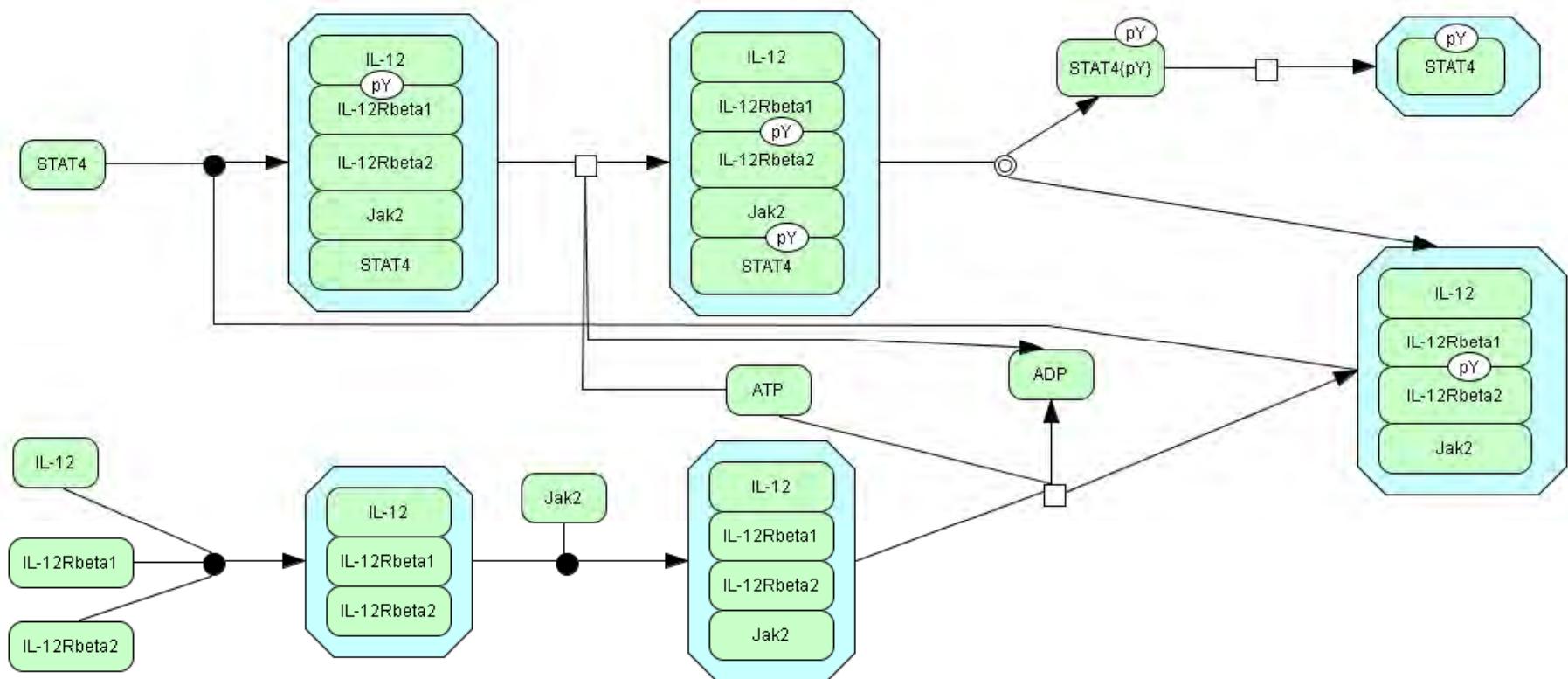
BioPAX – import dialog



BioPAX example (BioCyc)

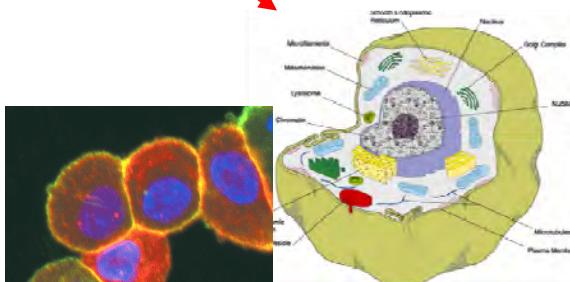
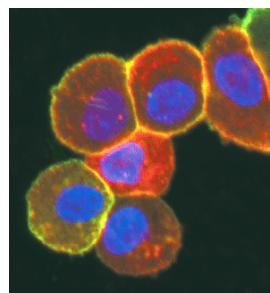


TRANSPATH example

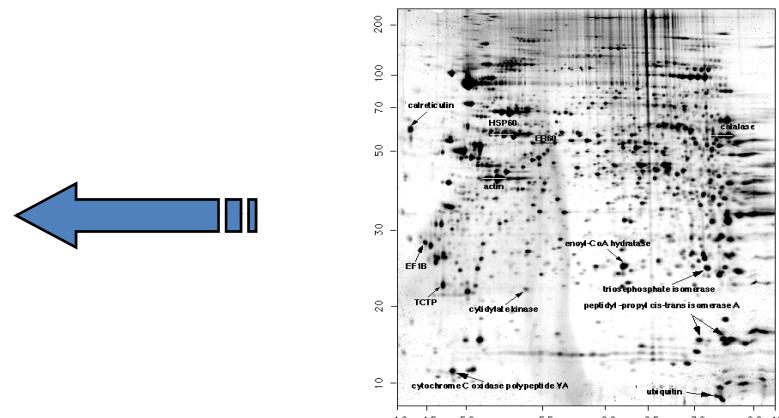


Human epidermoid carcinoma A431 cells treated by epidermal growth factor (EGF)

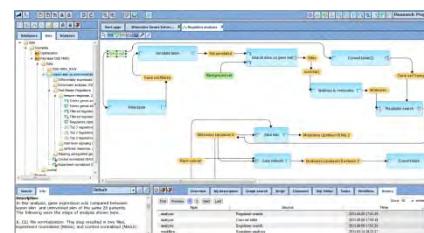
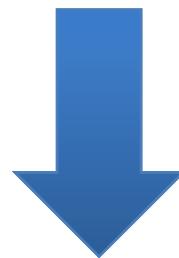
EGF ?



320 differentially expressed proteins



Master regulator analysis



EGF was still not in the list !



DNA is an active component
of biochemical networks.

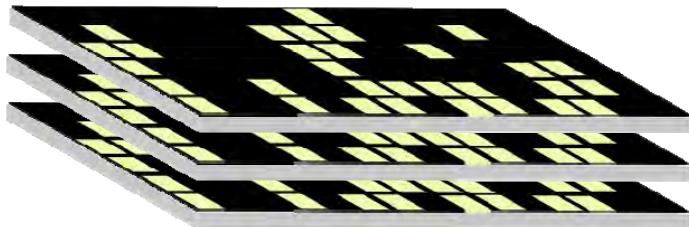
Network plasticity is a result
of epigenetic evolution during
cell development.

Epidermal Growth Factor induced Carcinogenicity

Philip Stegmaier¹, Alexander Kel¹, Edgar Wingender^{1,2}, and Jürgen Borlak³

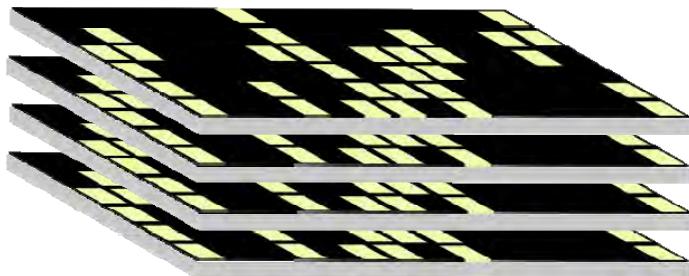
Hepatocellular transcriptome data of IgEGF-overexpressing mice

transgenic



transgenic/normal

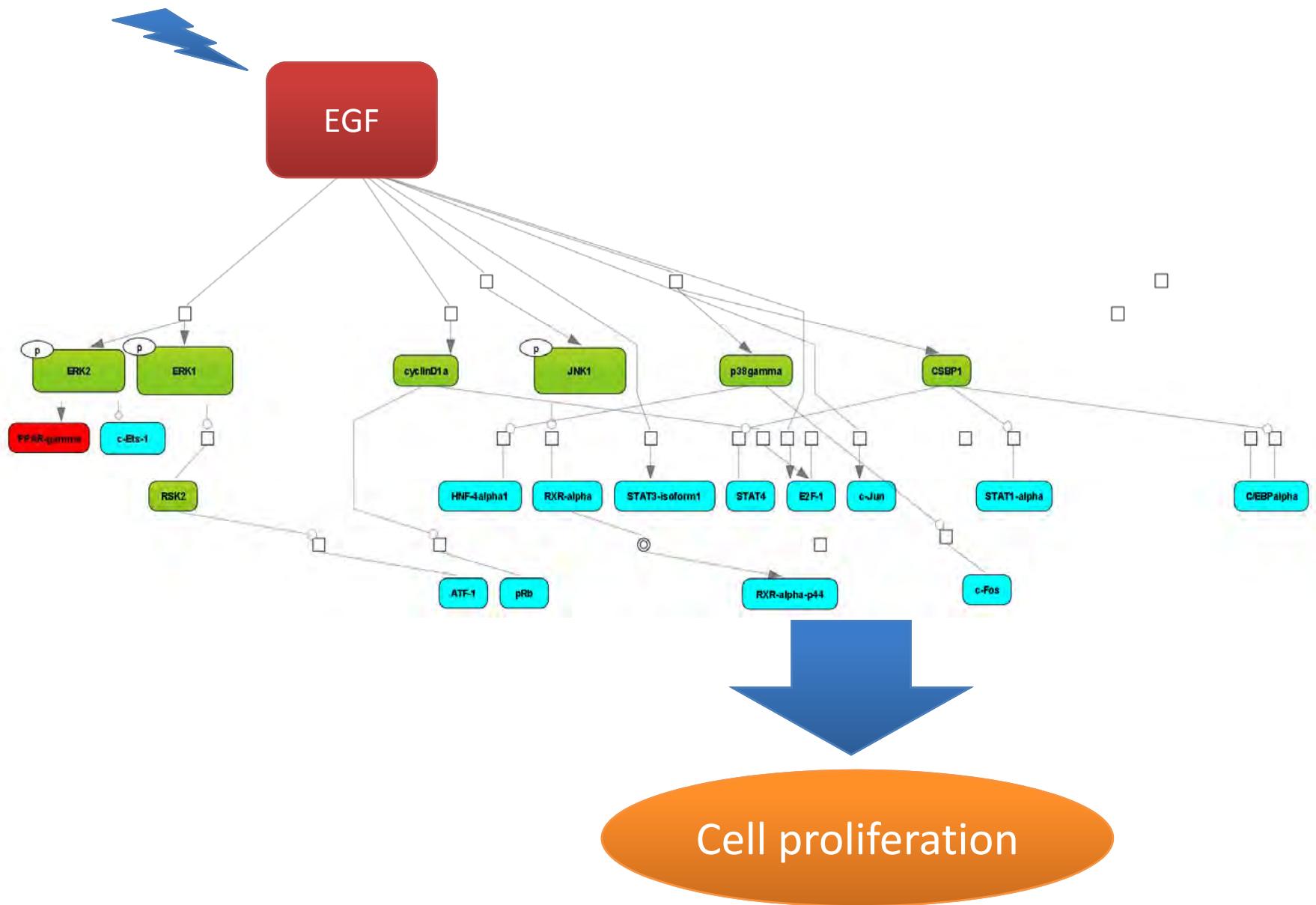
small tumor

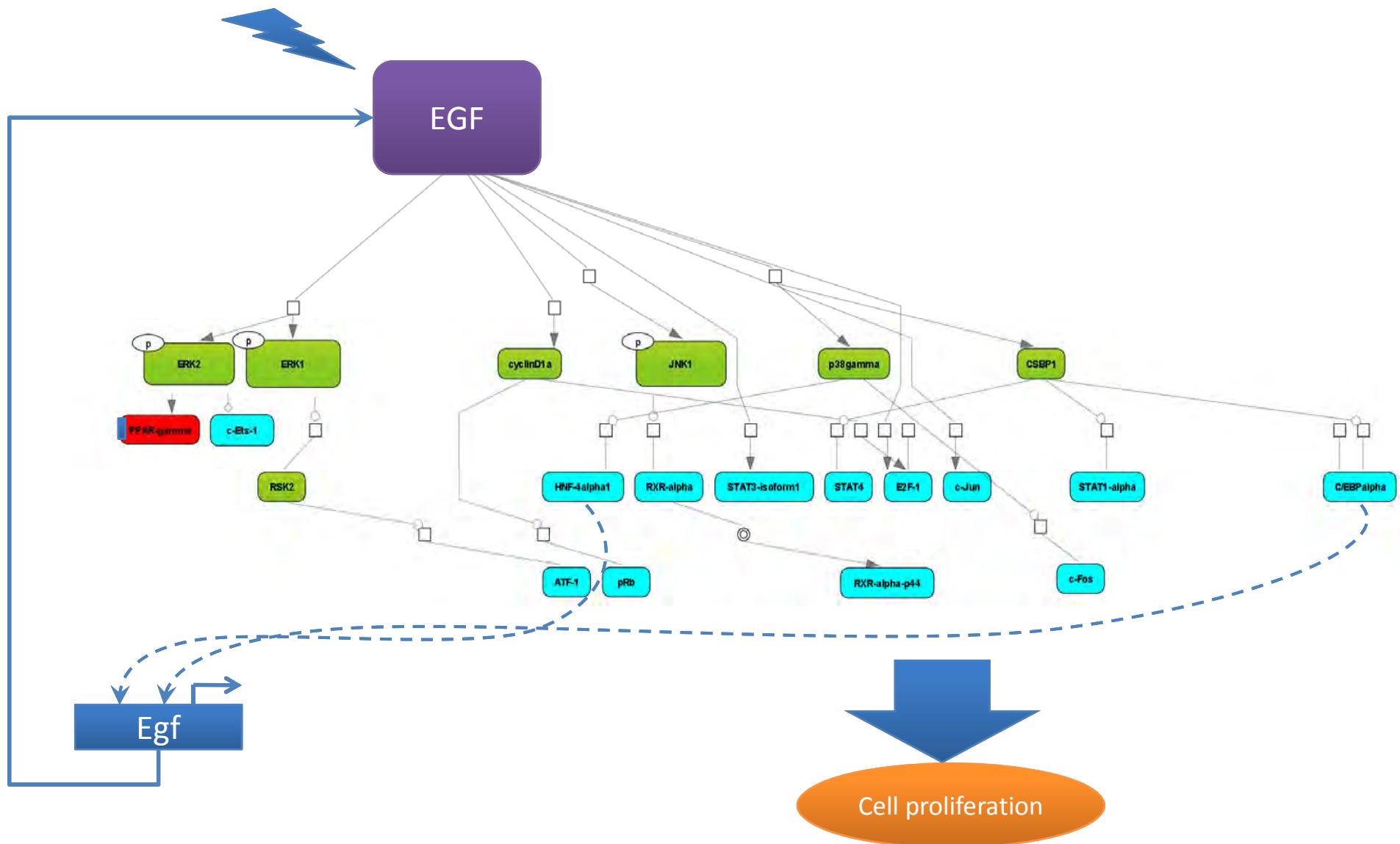


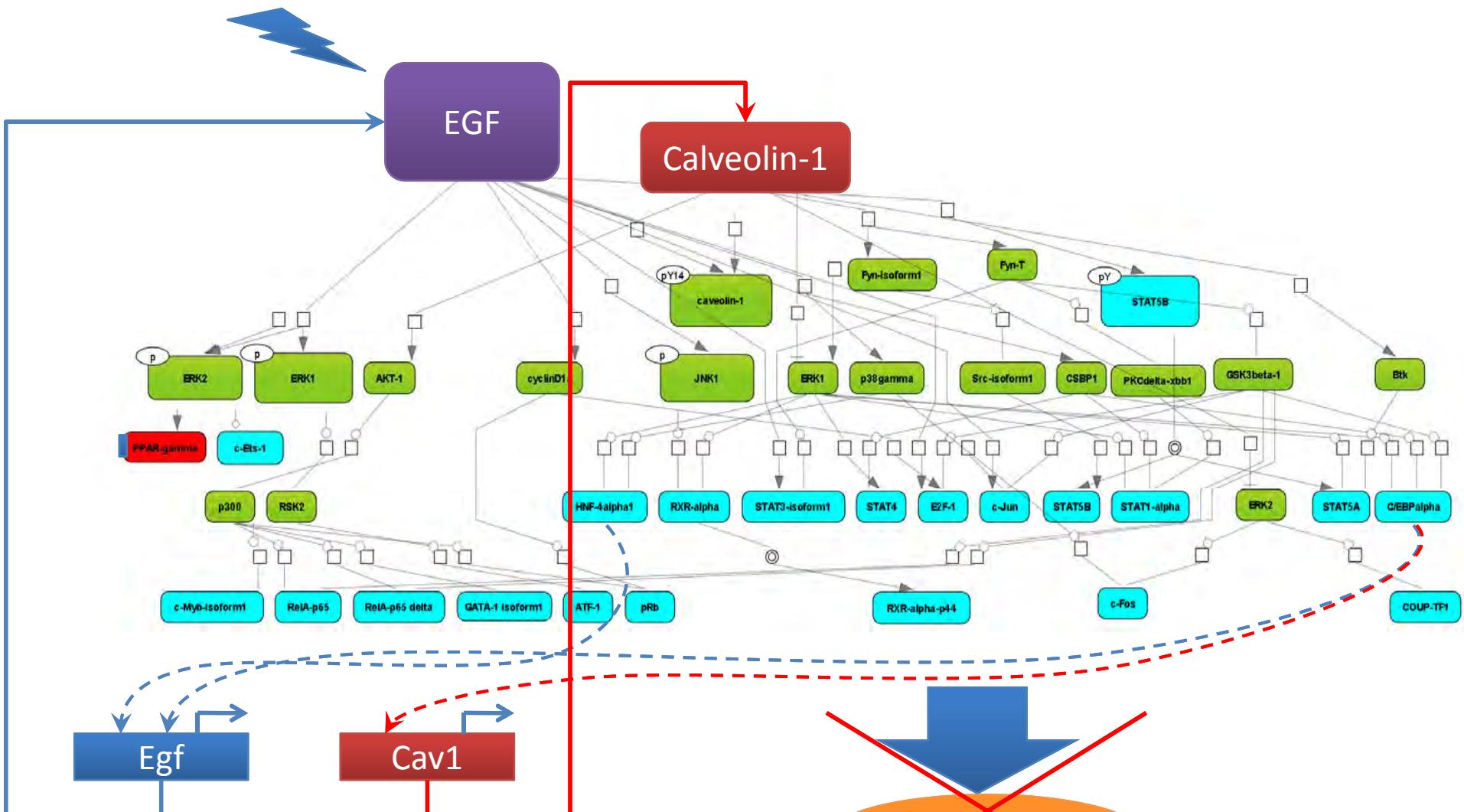
Tumoregenic
switch

small tumor/normal

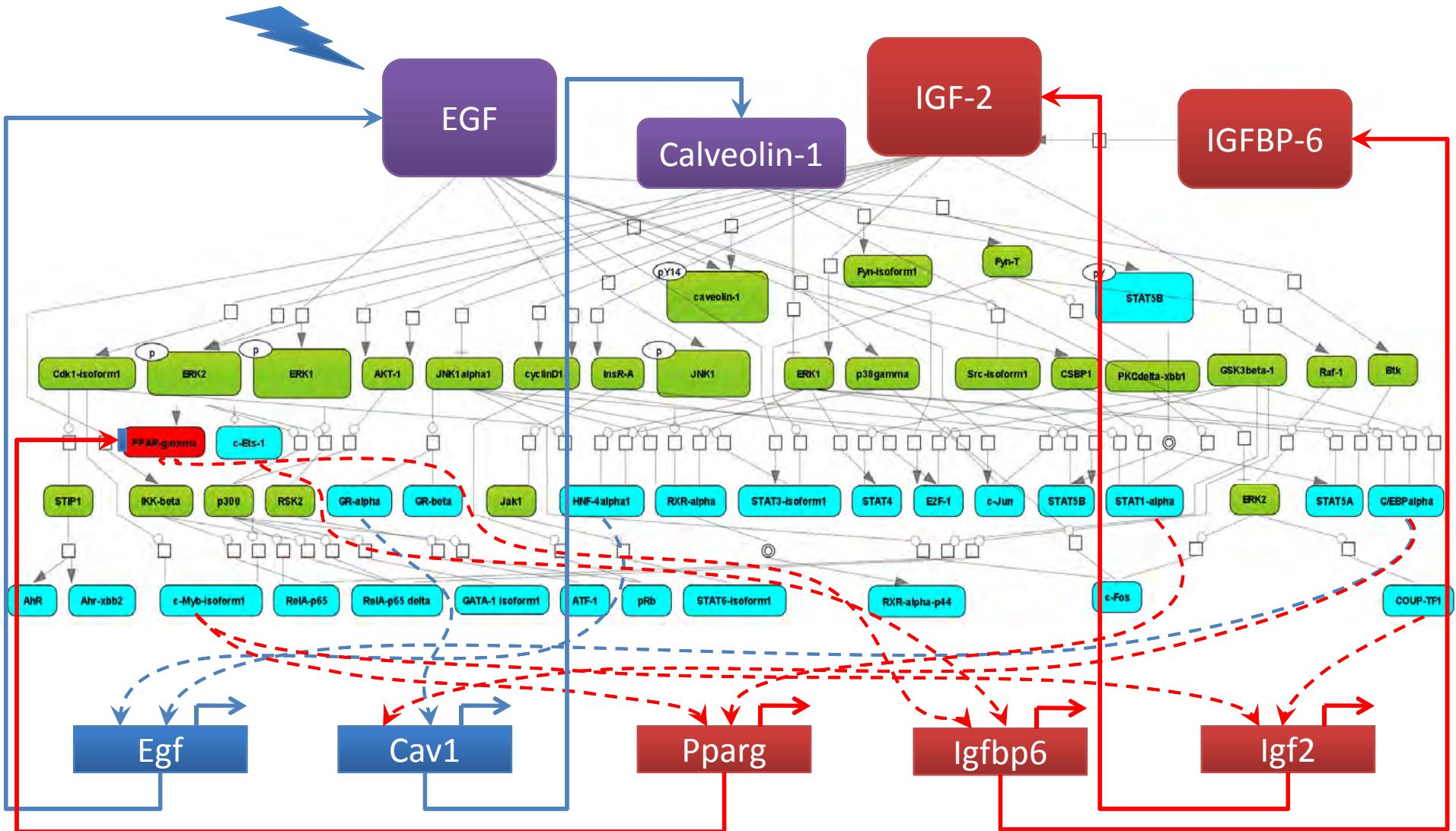


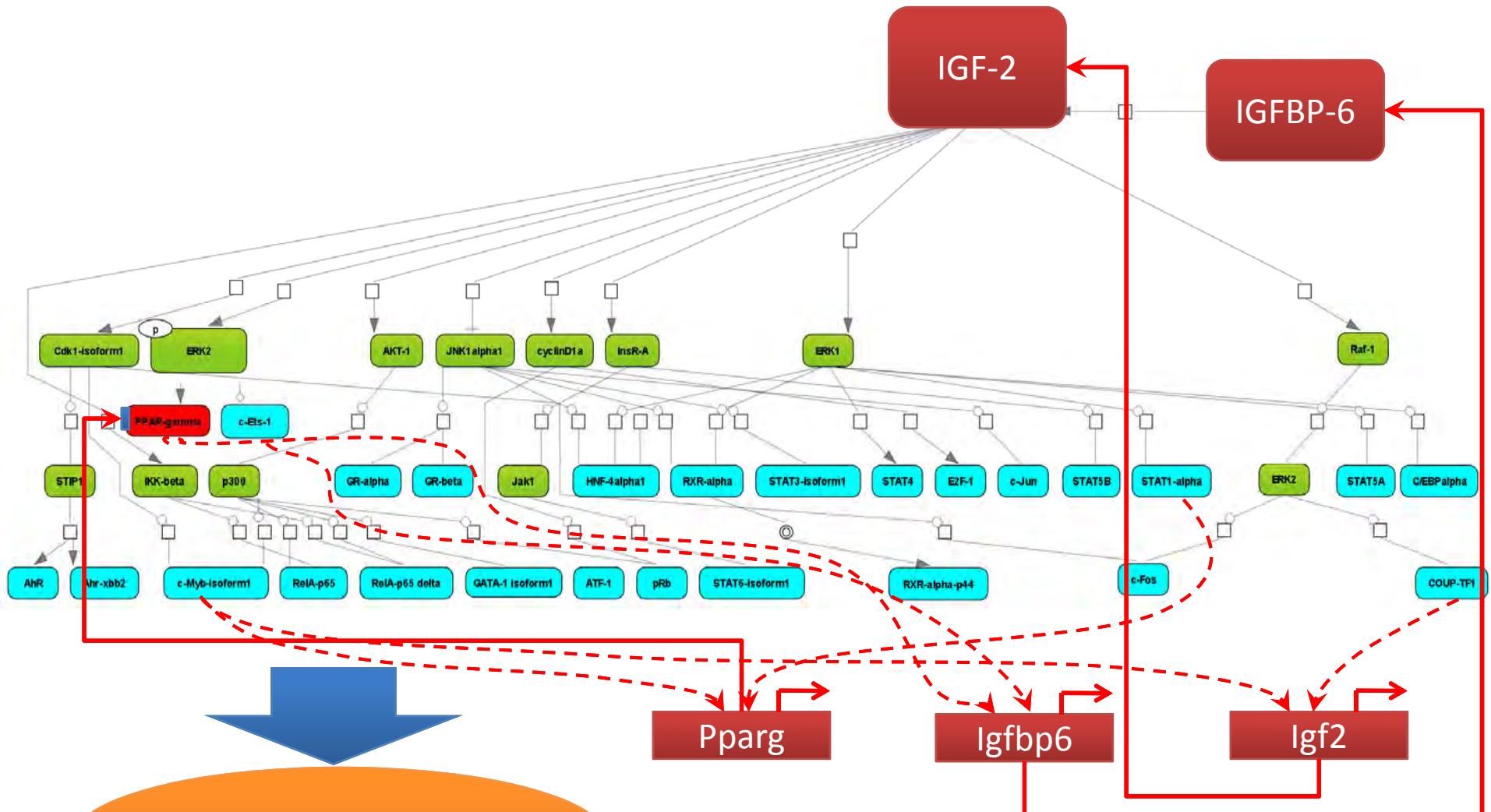






Cell proliferation





Cell proliferation

State concept

State describes changes between initial model and its variant:

- for simulation experiment (corresponds to SED-ML <changes>)
- for specific cell line or model conditions
- for history
 - history of editing can be represented as set of states
 - each state corresponds to some model build or commitment to repository.

State formalizes changes as following events:

- add element
- remove element
- change property.

Changes in the state can be grouped into transactions.

For example to remove reaction we need to remove reaction node and corresponding edges.

Changes can be presented as:

- table of changes, changes are grouped into transactions
- by decorating corresponding diagram elements

Internally, changes are core of BioUML undo/redo subsystem, that was further extended for the purposes above.

BioUML workbench

File Database Diagram Data Help

Databases \ Data \ Analyses \ Users \

- databases
 - + R000 Apoptosis model
 - + R000 Apoptosis models
 - + R000 Biopath
 - R000 Composite apoptosis model
 - Composite diagrams
 - CD95 signaling
 - Execution phase
 - TNF signaling
 - Diagrams
 - Bentele_2004
 - CD95 module
 - Caspase-8 module
 - Cytochrome C module
 - Mitochondrion module
 - NF-kB module
 - PARP module
 - Smac module
 - TNF module
 - TRAIL module
 - test
 - test_diagram
 - Simulation
 - Integrated model

Use journal name Research: Apoptosis

Composite apoptosis model : test_diagram \

state_1

This model was automatically converted from model BIOMD000000220 by using libSBML.

According to the [BioModels Database terms of use](#), this generated model is not related with model BIOMD000000220 any more.

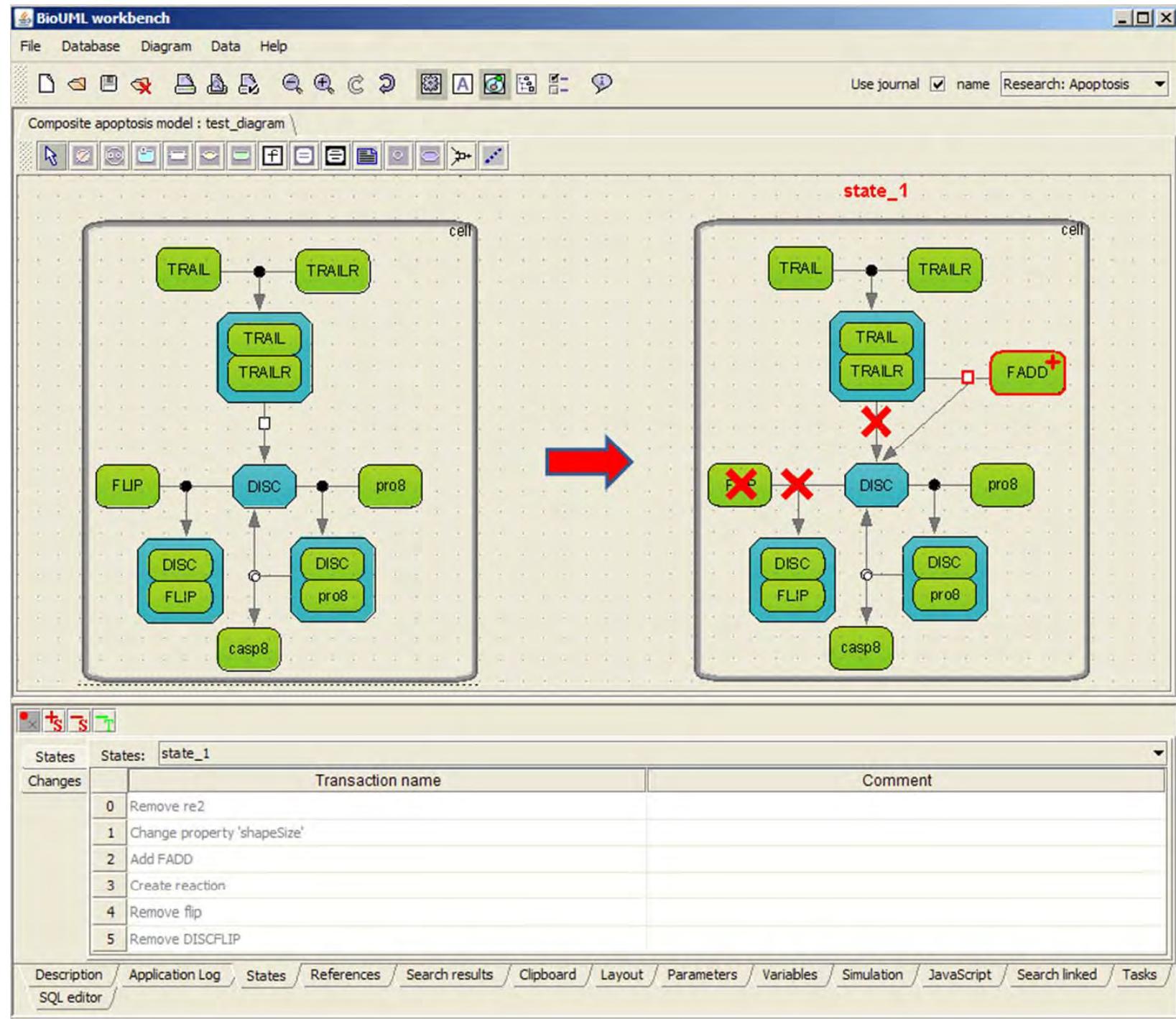
States States: state_1

Changes	Transaction name	Comment
0	Remove re2	
1	Change property 'shapeSize'	
2	Add FADD	
3	Create reaction	
4	Remove flip	

View Edit Editors

Description Application Log States References Search results Clipboard Layout Parameters Variables Simulation

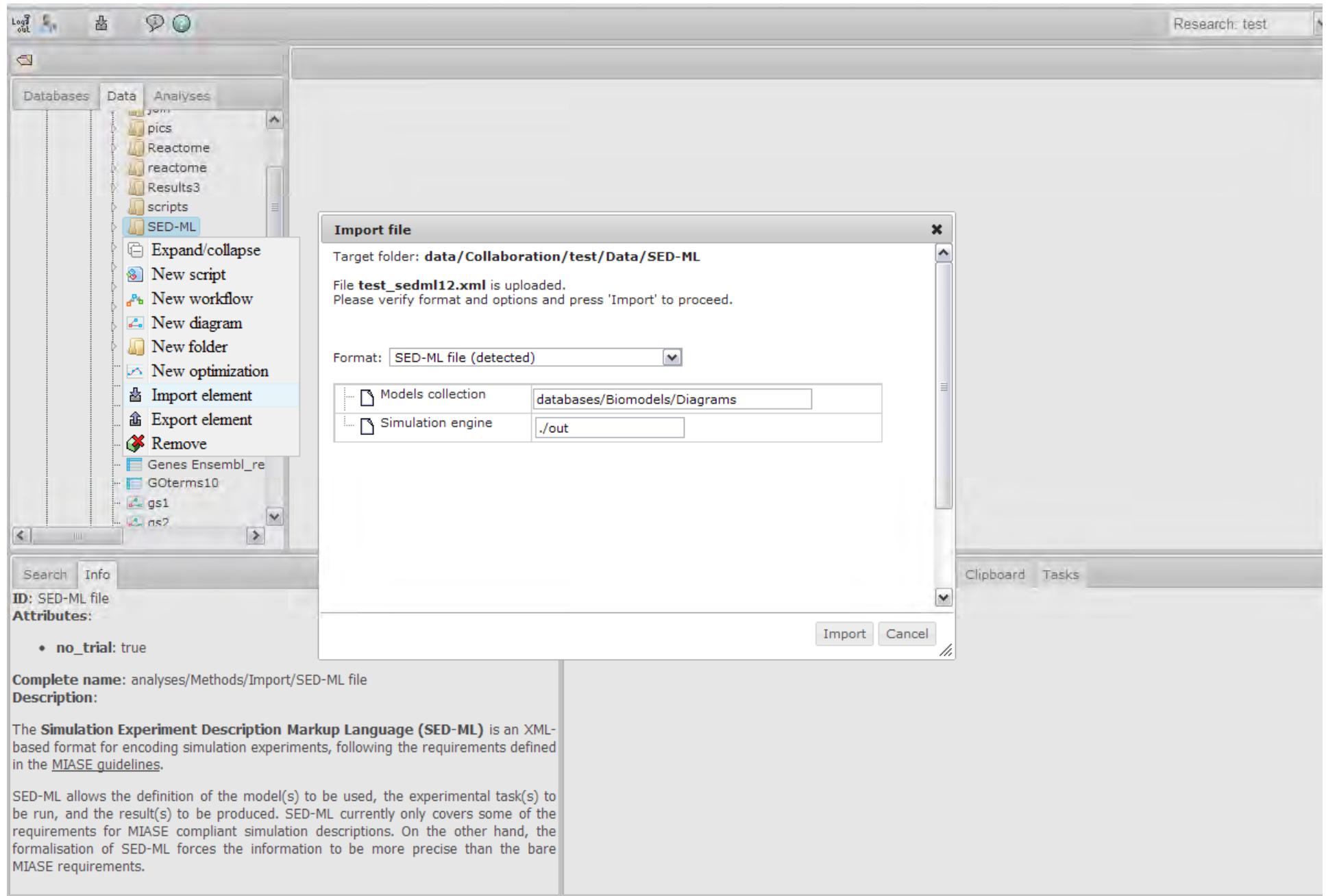
JavaScript Search linked Tasks SQL editor



SED-ML support

- SED-ML import
 - only SBML models are supported now
 - stored in user's project
- SED-ML changes presented as BioUML states
- SED-ML presented as workflow
- automated hierachic layout
- on-line simulation

SED-ML – import dialog



SED-ML workflow

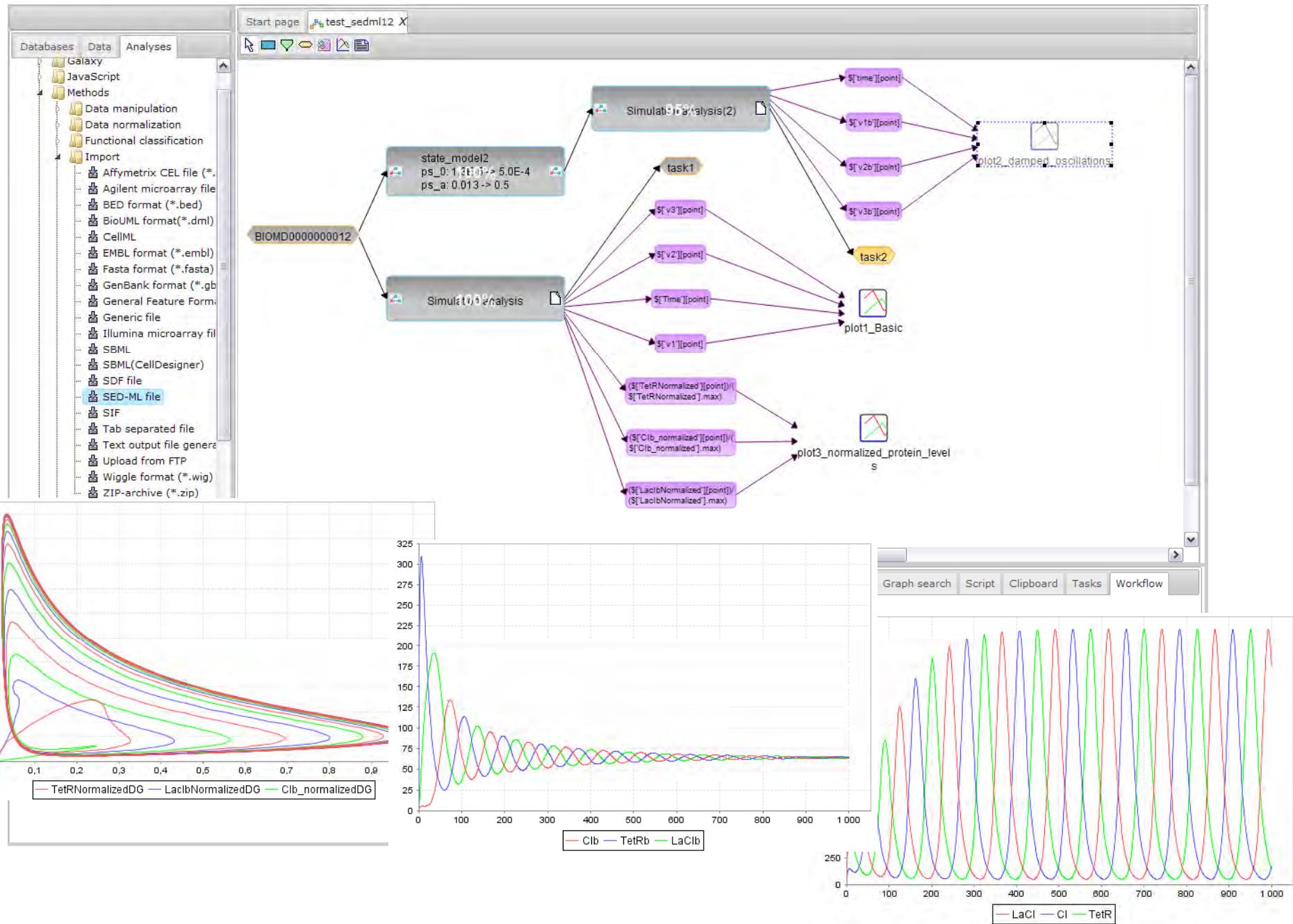
The screenshot illustrates a SED-ML workflow interface. The left sidebar shows a tree view of available analyses, including Galaxy, JavaScript, Methods (Data manipulation, Data normalization, Functional classification, Import), and SED-ML file. A specific SED-ML file named "BIOMD0000000012" is selected.

The main workspace displays a workflow graph. A central node labeled "Simulation analysis" has multiple outgoing arrows pointing to various tasks and plots. One task, "task1", contains expressions like $(\$[LacIbNormalized][point])/([\$[LacIbNormalized].max])$ and $(\$[TerRNormalized][point])/([\$[TerRNormalized].max])$. Another task, "task2", contains expressions like $(\$[Cib_normalized][point])/([\$[Cib_normalized].max])$. The results of these tasks are plotted as "plot1_Basic" and "plot3_normalized_protein_level_s".

The "state_model2" node contains parameter definitions: $ps_0: 1.3E-5 \rightarrow 5.0E-4$ and $ps_a: 0.013 \rightarrow 0.5$.

The bottom panel provides detailed information about the selected SED-ML file, including its ID, attributes (e.g., no_trial: true), complete name, and description. It also lists the MIASE guidelines and the XML-based nature of SED-ML. The "Workflow" tab is active, showing simulation parameters: Model (set to "...models/Diagrams/BIOMD0000000012"), Simulator name (JVode), Initial time (0.0), Completion time (1000.0), Time increment (1.0), Skip points (0), Output start time (0.0), and Simulation result (data/Collaboration/test/tmp/task1).

Simulation



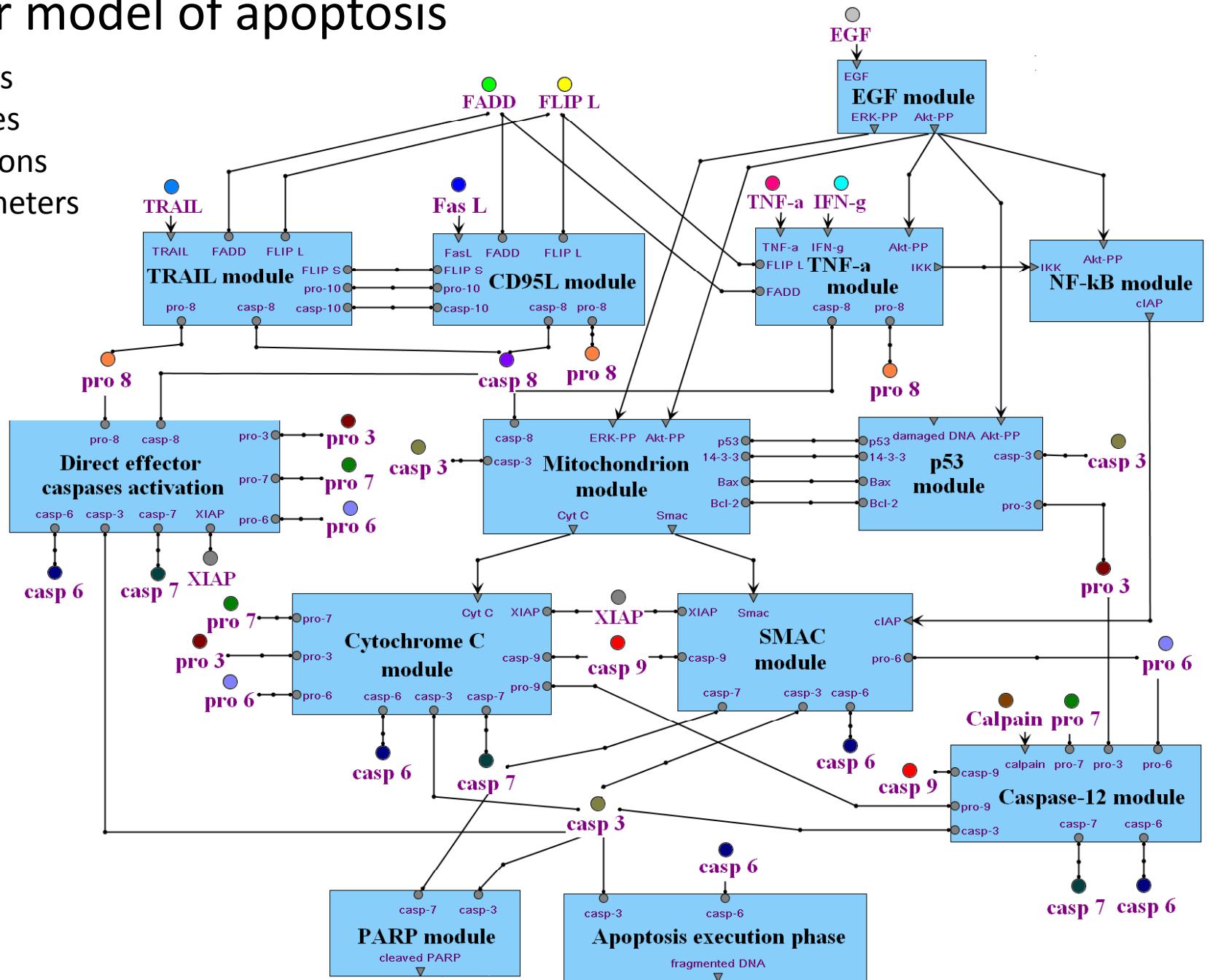
Modular modelling

Composite model
of the Apoptosis Machinery

Agent based model
of arterial blood pressure regulation

Modular model of apoptosis

- 13 modules
- 286 species
- 684 reactions
- 719 parameters



EGF module

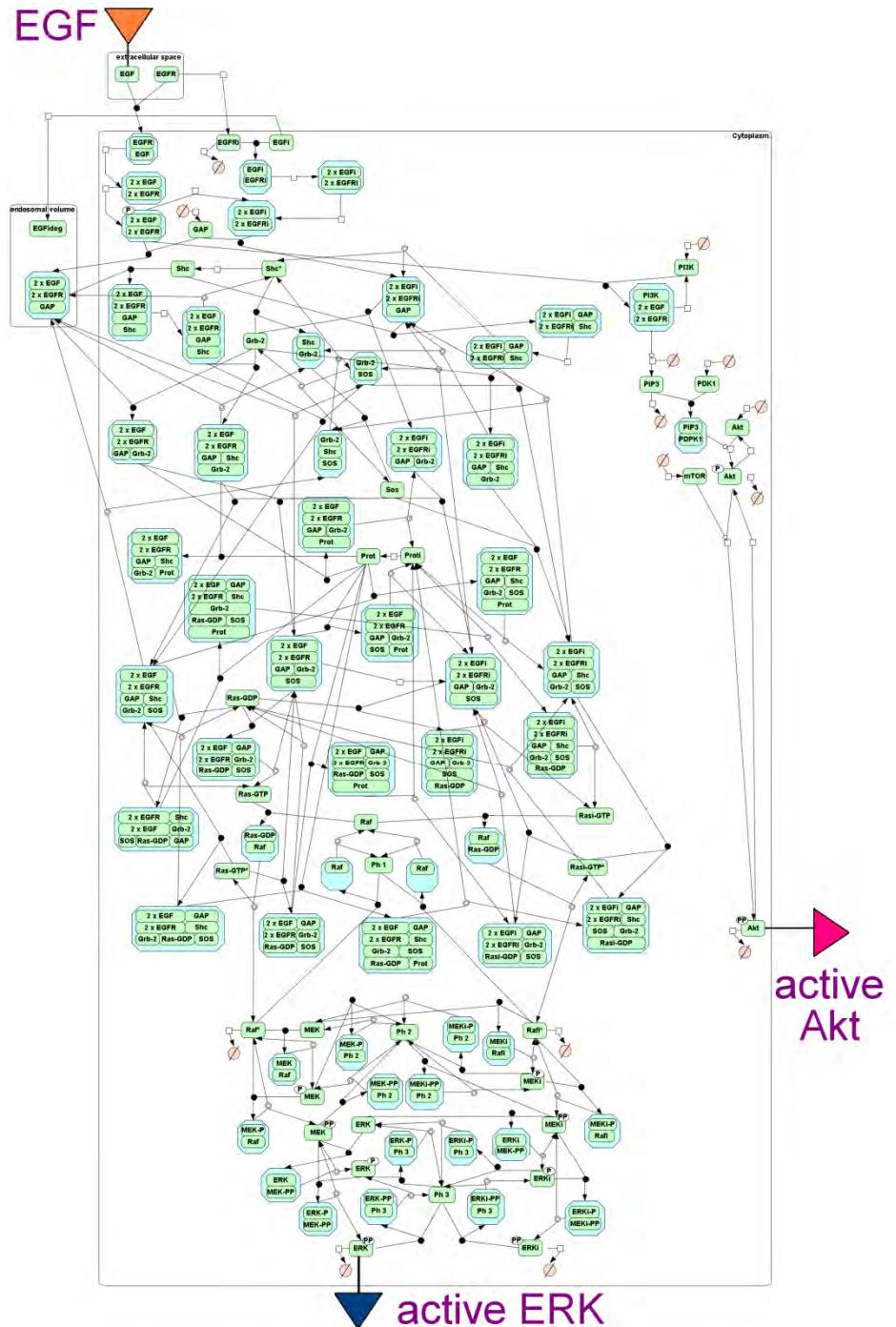
(BMOND ID: Int_EGF_module)

Schoeberl B, et al: *Nature Biotechnology* 2002

Borisov N, et al: *Molecular Systems Biology* 2009

Additions:

- ✓ Reactions of protein syntheses and degradations



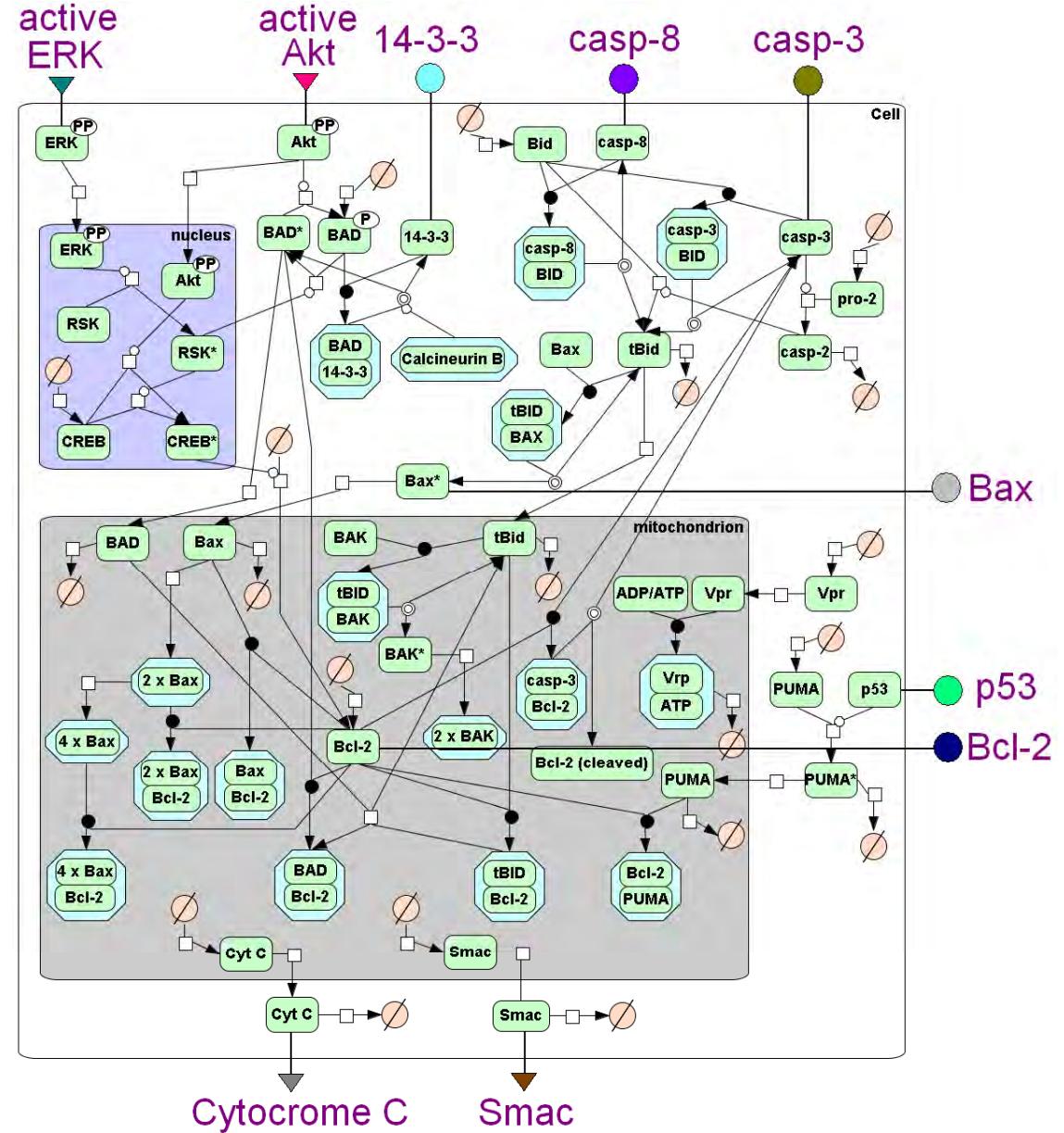
Mitochondron module

(BMOND ID: Int_Mitoch_module)

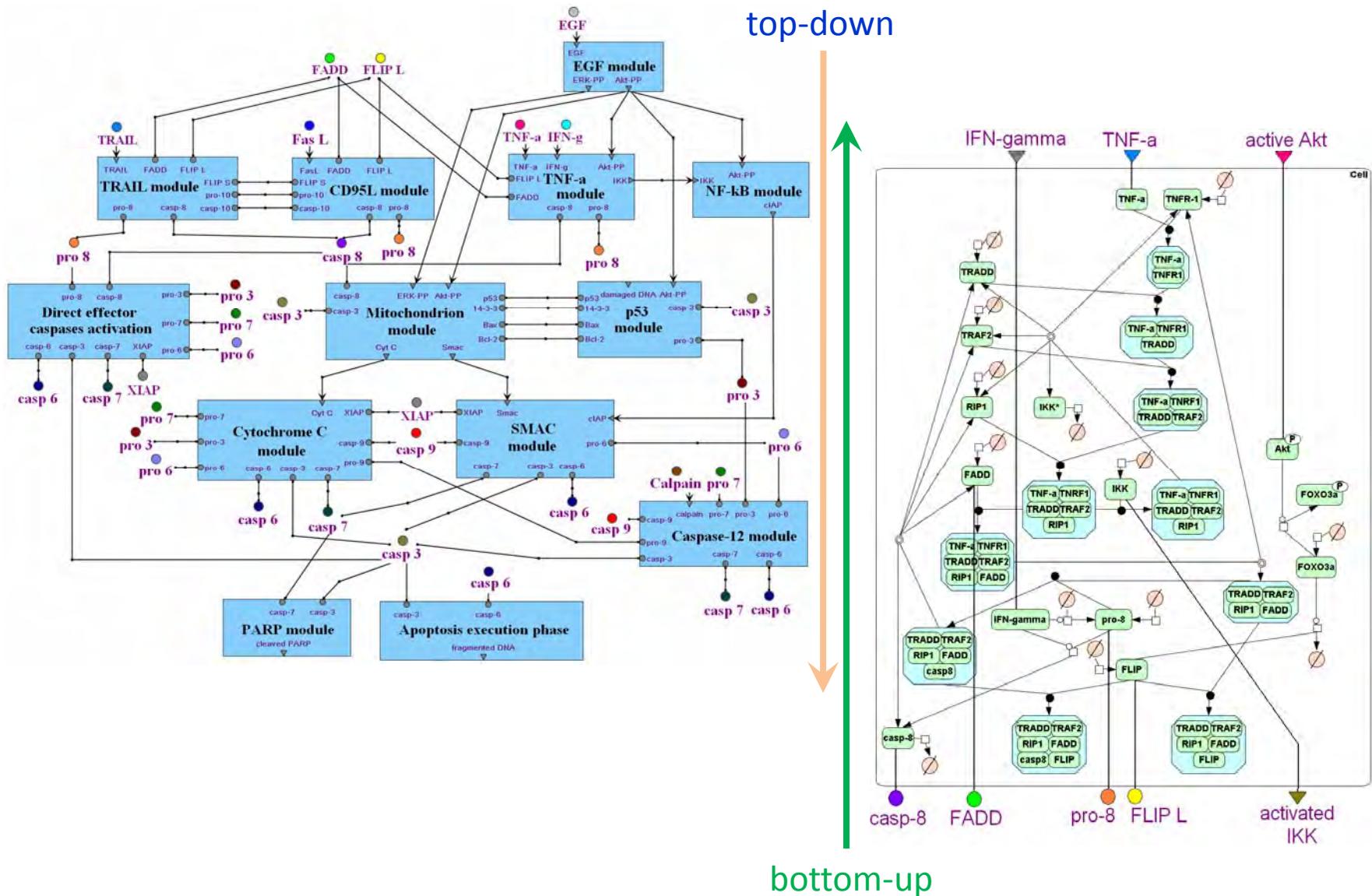
Bagci EZ, et al,
Biophysical J 2006
Albeck JG, et al,
PLoS Biol 2008

Additions:

- ✓ Activation of CREB and deactivation of BAD by Akt-PP and ERK-PP
- ✓ Upregulation of Bcl-2 by CREB
- ✓ Bcl-2 suppression by p53



Modular model allows us to combine both up-down and bottom-up approaches

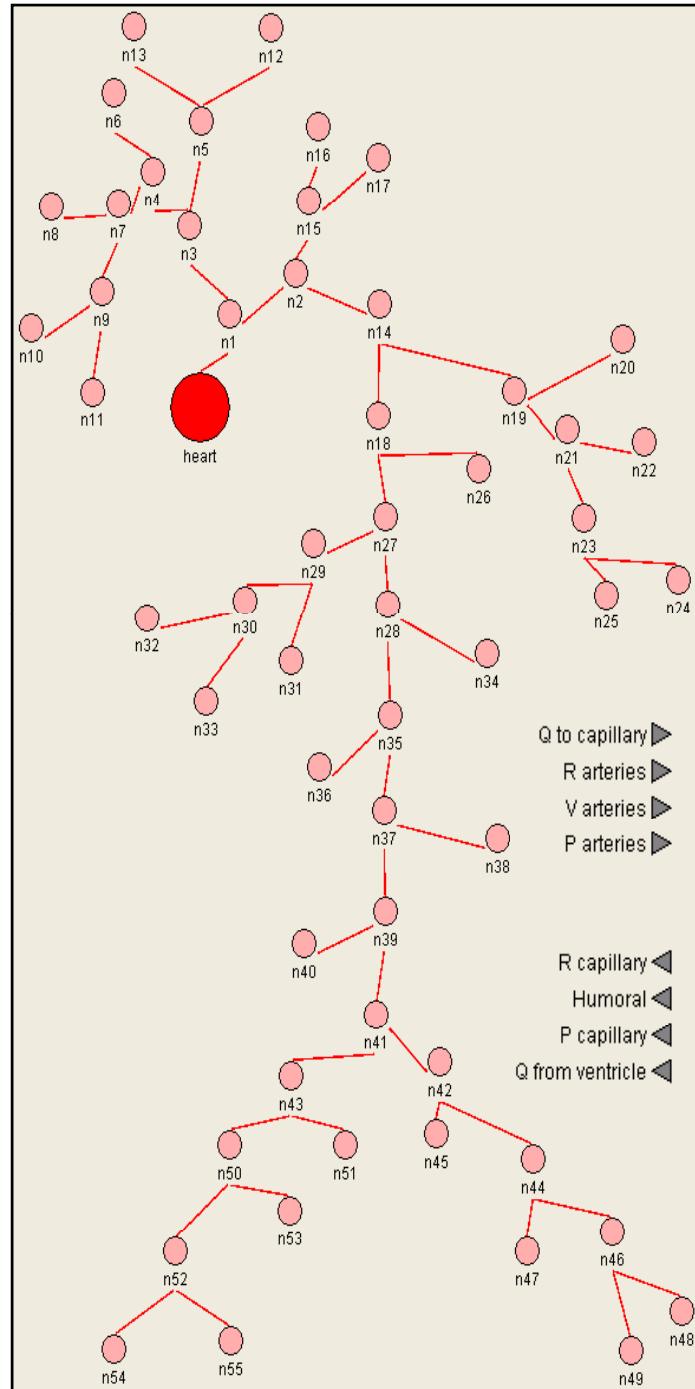


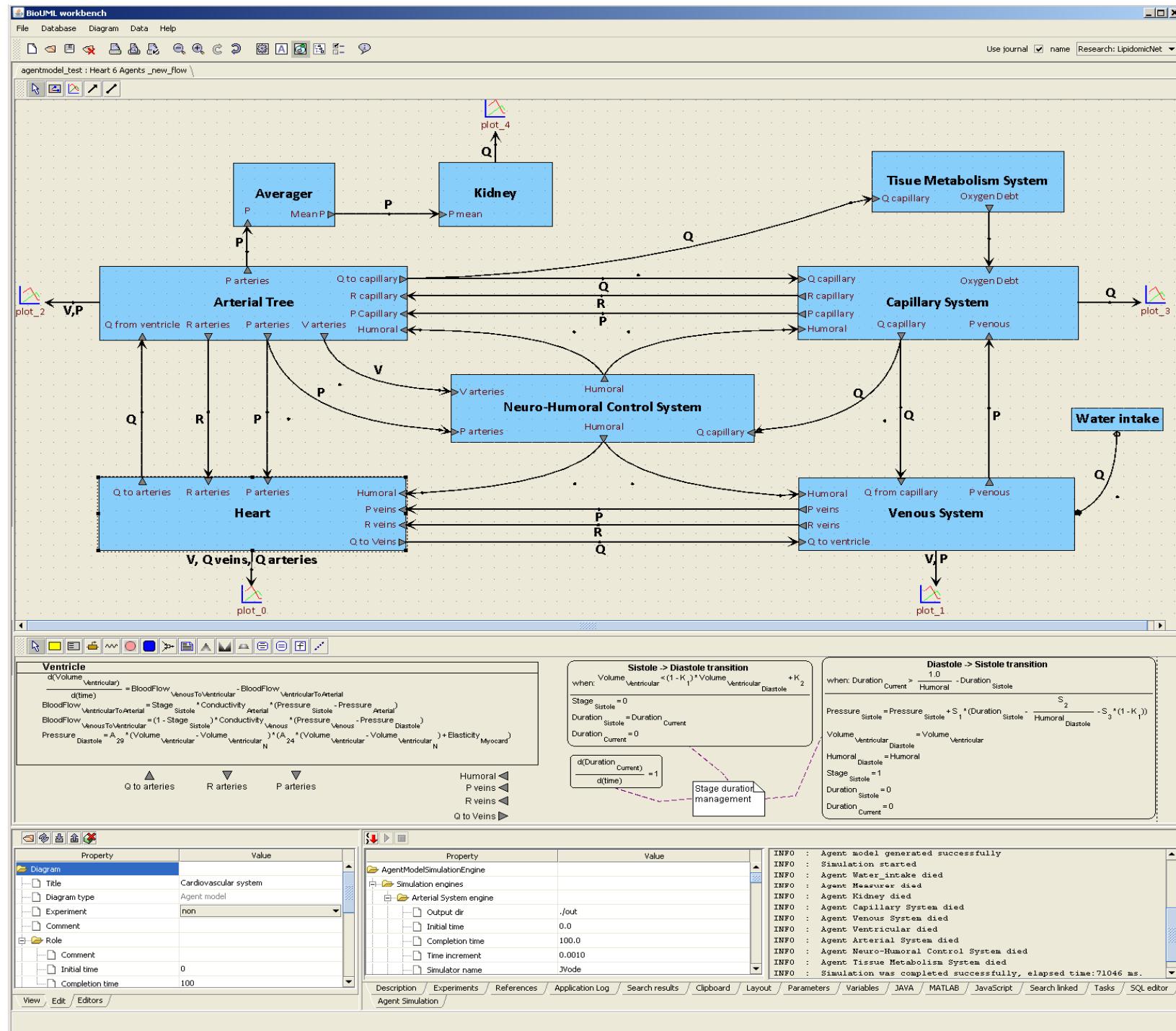
Agent based modeling

- Ascape library is used
- main type of agents:
 - ODE agent
 - arterial tree
 - plot

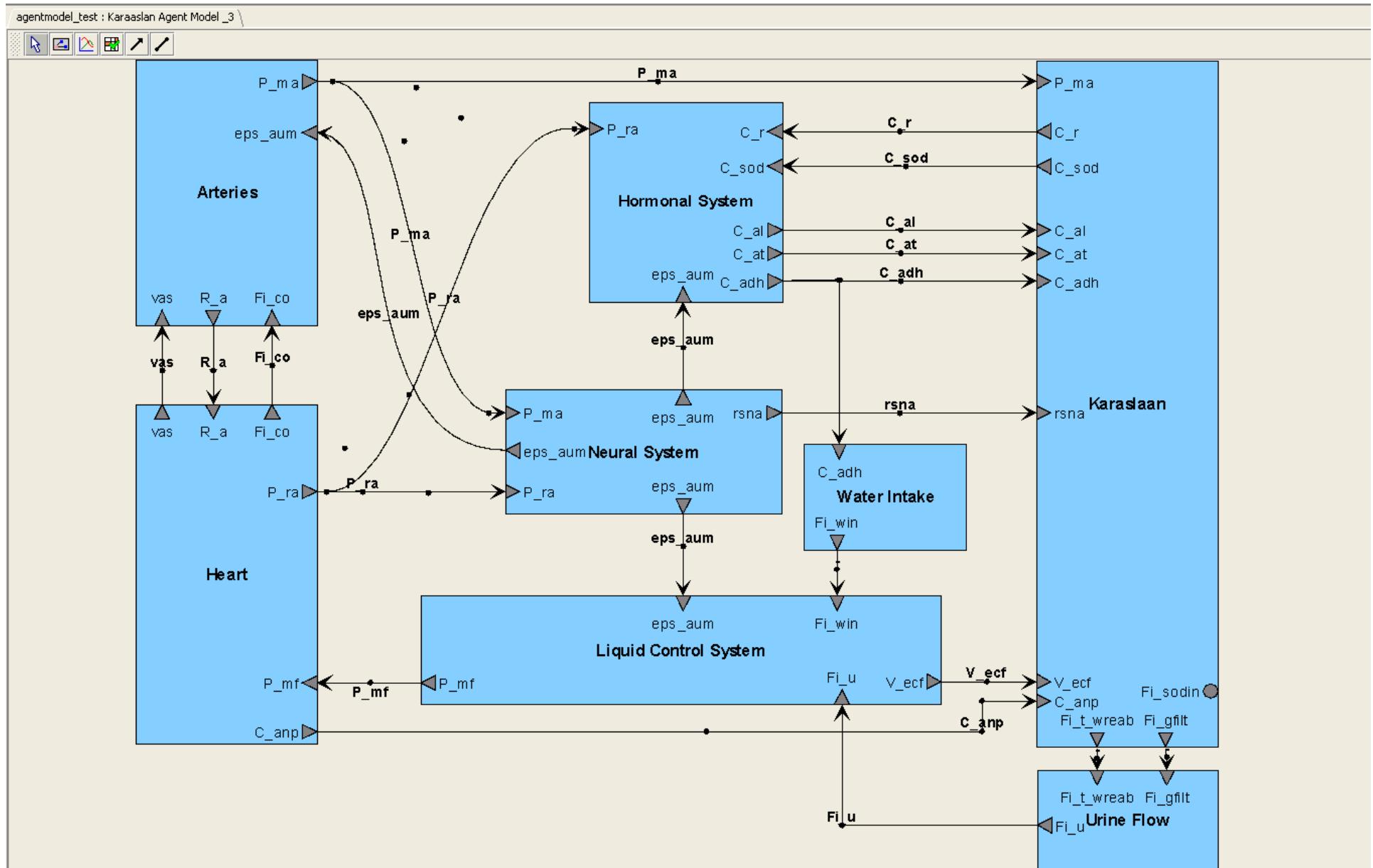
Arterial Tree PDE agent

Legend:
P – Pressure
R – Resistance
Q – Blood Flow
V – Volume





Blood arterial pressure regulation: another build



Systems biology: reproducible highthroughput data analyses

- analyses: algorithms, scripts, workflows
- integration with R/Bioconductor, Galaxy
- data: microarrays, NGS, ChIP-SEQ
- visualization: genome browser

Systems biology: reproducible highthroughput data analyses

- 1) analysis dialog
- 2) scripts
 - JavaScript, R
 - script editor, console
- 3) workflows

Firefox ▾

Affymetrix normalization - geneXplain 1.... +

http://platform.genexplain.com/bioumlweb/#de=analyses/Methods/Data normalization/Affymetrix nor

Yahoo! Search SEARCH 60° Google

Research: Sysco

Databases Data Analyses

Analyses

- JavaScript
- Methods
 - Data manipulation
 - Data normalization
 - Affymetrix normalization
 - Agilent normalization
 - Illumina normalization
 - Normalize Affymetrix experiment and control
 - Normalize Agilent experiment and control
 - Normalize Illumina experiment and control
 - Functional classification
 - Import
 - Molecular networks
 - Optimization
 - Sequence manipulation
 - Simulation
 - Site analysis
 - Statistical analysis
 - CRC clustering
 - Correlation Analysis
 - Fold-Change calculation
 - Hypergeometric analysis
 - K-means clustering
 - Meta analysis
 - Polynomial Regression analysis

Start page Affymetrix normalization X

CEL files	[?]	[0]
Method	[?]	MASS
Background correction	[?]	MAS
Normalization method	[?]	quantiles
PM correction	[?]	pmonly
Summarization	[?]	mas
CDF version	[?]	(select element)
Output name	[?]	data/Normalized (MAS5)

Run

Search Info Default

Affymetrix Normalization

Normalization of Affymetrix CEL files based on the functions of the Bioconductor AFFY package.

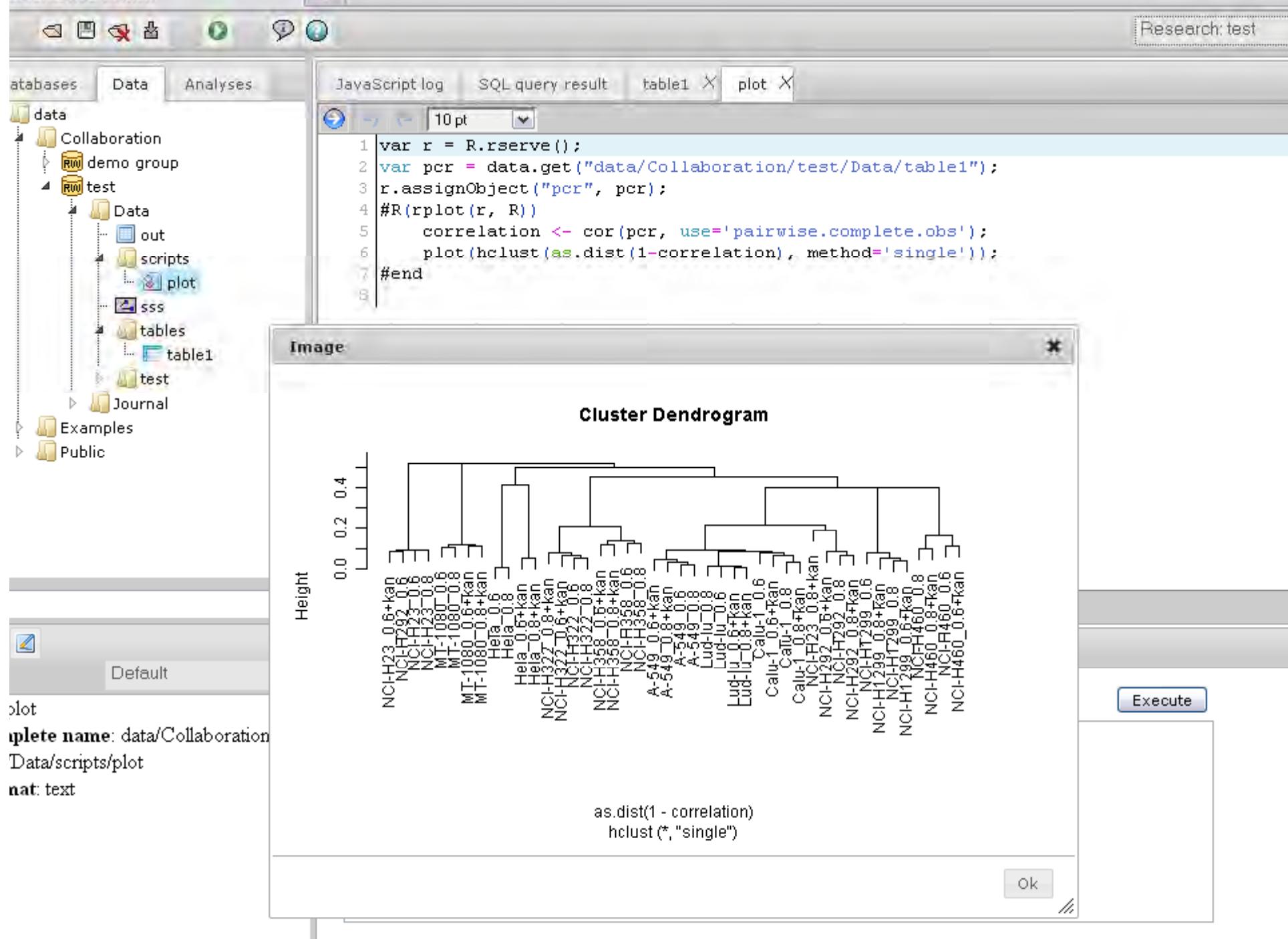
User description is not available

http://platform.genexplain.com/bioumlweb/#search_tab_container

JavaScript host objects allows to merge R/Bioconductor and Java/BioUML worlds



```
1 var r = R.rserve();
2 var pcr = data.get("data/Collaboration/test/Data/table1");
3 r.assignObject("pcr", pcr);
4 #R(rplot(r, R))
5     correlation <- cor(pcr, use='pairwise.complete.obs');
6     plot(hclust(as.dist(1-correlation), method='single'));
7 #end
```



http://localhost:8080/bioumlweb/#de=data/Collaboration/test/Data/New workflow

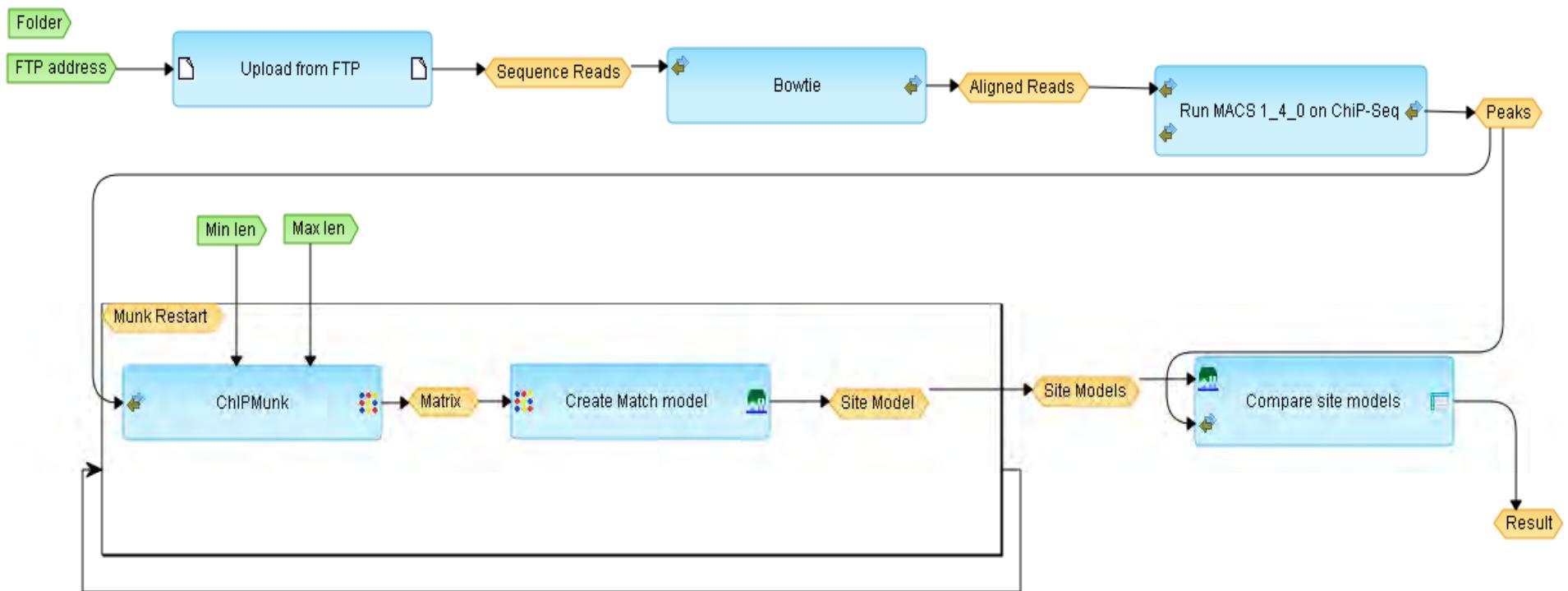
Start page New workflow X

The screenshot shows a web-based bioinformatics workflow editor. On the left, a sidebar lists categories like Databases, Data, Analyses, and Users. Under Analyses, the 'Methods' section is expanded, showing various data processing tools. One tool, 'Convert table', is selected and highlighted in blue. The main workspace displays a workflow diagram with three nodes: 'Input' (green), 'Convert table' (blue), and 'Output' (yellow). Arrows indicate the flow from Input to Convert table, and from Convert table to Output. Below the diagram, a detailed configuration panel is open for the 'Convert table' analysis. It includes tabs for Search, Info, Default, SQL Editor, Tasks, Workflow, and History. The 'Info' tab is active, showing the ID as 'Convert table', the complete name as 'analyses/Methods/Data/Convert table', and a description area. A bold section titled 'Convert table identifiers using BioHub(s)' provides a detailed explanation of the analysis's function. The 'SQL Editor' tab contains a table with configuration parameters:

Name	Input
Type	Data element
Value	data/Collaboration/test
Default value	\$project\$/Data ...
Role	Input
Element type	Table
Reference type	Unspecified
Rank (sort order)	1

- Single source ID matches to several target IDs. In this case source row will be copied several times, one copy per one target ID.
- Source ID doesn't match to any target ID. In this case source row

ChIP-seq processing pipeline



Galaxy – analyses methods

The screenshot shows the Galaxy web interface with the URL 46.137.177.212/bioumlweb/#de=analyses/Galaxy/motifs/rgweblogo3. The interface is divided into several panels:

- Top Bar:** Includes standard browser controls (Back, Forward, Stop, Refresh), a search bar with the URL, and a "Research: demo" dropdown.
- Left Sidebar:** A tree view of available tools under "Analyses". The "Sequence Logo" tool is selected and highlighted in blue.
- Central Panel (rgweblogo3 Configuration):** This panel contains the configuration form for the rgweblogo3 tool. It includes:
 - A left sidebar with options: Fasta File, Include entire sequence (default) or specify a subsequence range to use, Output format for image (or text report), Output weblog size, Colour scheme for output Sequence Logo, logoname, and output.
 - A right sidebar with dropdown menus and input fields: (select element) for Fasta File, complete sequence for Include entire sequence, PNG screen quality for Output format, Large for Output weblog size, Default automatic colour selection for Colour scheme, and (select element) for logoname and output.
 - A "Run" button at the bottom.
 - A large empty rectangular area below the run button, likely for displaying the generated sequence logo image.
- Bottom Left Panel (Tool Details):** This panel displays detailed information about the rgweblogo3 tool.
 - Search, Info, Default Buttons:** Standard search and info buttons.
 - ID:** rgweblogo3
 - Complete name:** analyses/Galaxy/motifs/rgweblogo3
 - Description:** User description is not available.
 - Note:** This tool uses Weblogo3_ in Galaxy to generate a sequence logo. The input file must be a fasta file in your current history.
 - Usage Note:** It is recommended for (eg) viewing multiple sequence alignments output from the clustalw tool - set the output to fasta and feed it in to this tool.
 - Output Example:** A typical output looks like this:

```
.. image:: ./static/images/rgWebLogo3_test.jpg
```
 - Warning:** **Warning about input Fasta format file**
- Bottom Right Panel (Tool Buttons):** Includes buttons for My description, Graph search, Script, Clipboard, and Tasks.

Galaxy - workflow

The screenshot shows the Galaxy web interface for a ChIP-seq workflow. The top navigation bar includes links for Log out, Help, and Research: demo. The main workspace displays a workflow graph and a detailed view of a specific tool configuration.

Workflow Graph:

```
graph LR; A[ChIP-Seq Tags] --> B[peakcalling_ccat]; C[ChIP-Seq Control Tags] --> B; B --> D[Peaks]; D --> E[Annotation_Profiler_0]; E --> F[Annotated Sites]; E --> G[meme_meme]; G --> H[Meme report]
```

Tool Configuration (meme_meme):

ID: meme_meme
Title: meme_meme
Size: 10
Attributes:

- analysisName: meme_meme
- innerNodesPortFinder: true
- parameter.non_commercial_use: false
- parameter.options_type.advanced.maxiter: 50
- parameter.options_type.advanced.nmotifs: 1
- parameter.options_type.dna.pal: false
- parameter.options_type.dna.revcomp: false
- parameter.options_type.exact.width: 10
- parameter.options_type.min_max_sites.maxisites: 50
- parameter.options_type.min_max_sites.minsites: 1
- parameter.options_type.nsites.nsites: 1
- parameter.options_type.pam.spfuzz: 120
- parameter.options_type.range.maxw: 50
- parameter.options_type.range.minw: 8
- parameter.options_type.trim.noendnans: false

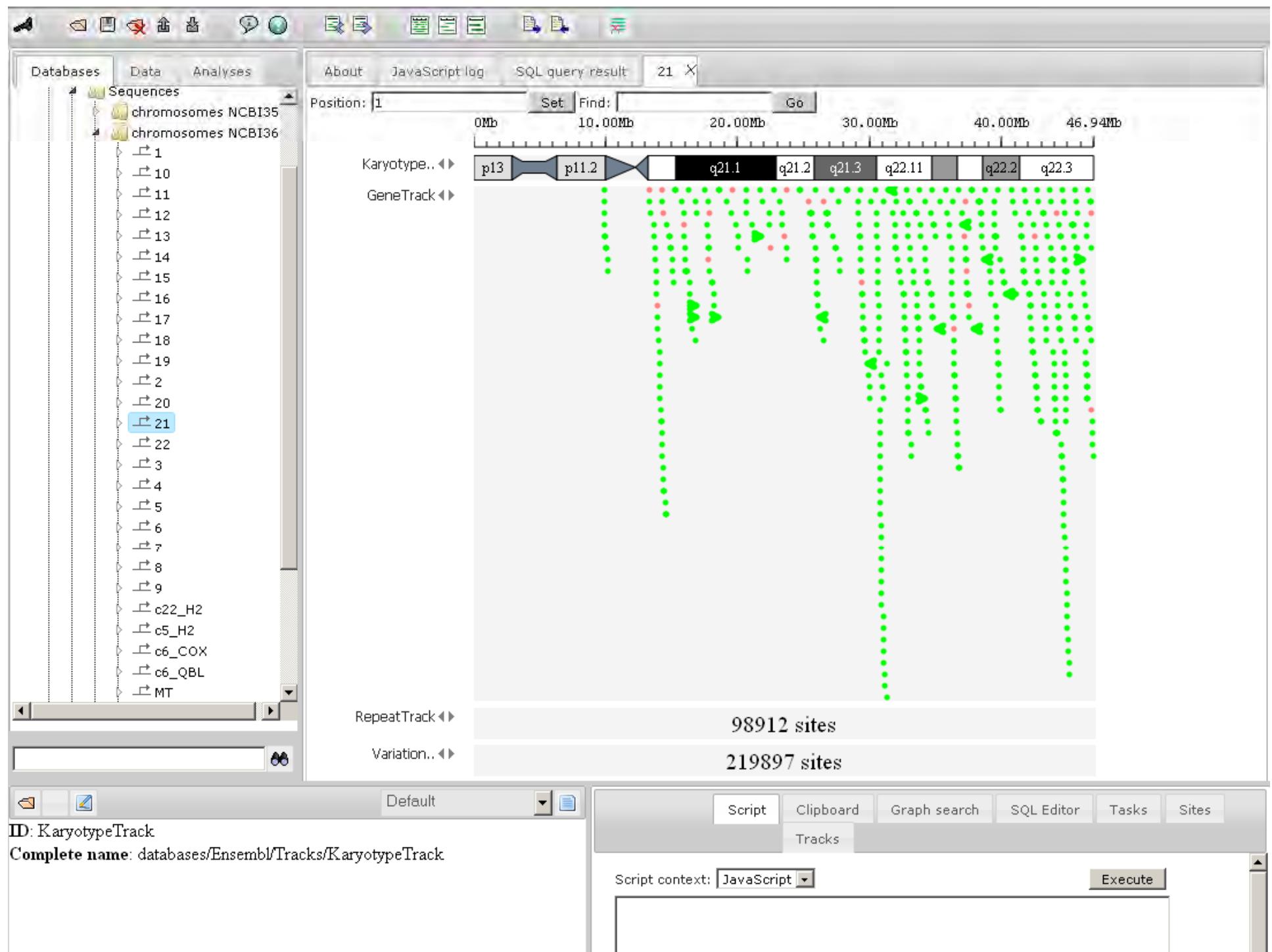
Tool Configuration (Annotation_Profiler_0):

I certify that I am not using this tool for commercial purposes.	<input type="checkbox"/>
Options Configuration	Basic
Sequences	(select element)
txt_outfile	out/
xml_outfile	out/
html_outfile	(select element)

Genome browser

Genome browser: main features

- uses AJAX and HTML5 <canvas> technologies
- interactive - dragging, semantic zoom
- tracks support
 - Ensembl
 - DAS-servers
 - user-loaded BED/GFF/Wiggle files



The screenshot shows the UCSC Genome Browser interface. The left sidebar displays a tree view of databases and tracks. The main panel shows a genomic track for chromosome 21, starting at position 35332750 and ending at 35332840. The track includes several data layers: Karyotype (showing banding patterns), GeneTrack (listing genes like RUNX1), RepeatTrack (showing trf repeats as green arrows), and Variation (showing SNPs with IDs like rs62218489, rs10587256, and rs62641634). A blue box highlights the '21' track in the sidebar.

site

siteID: 462

Sequence name: 21

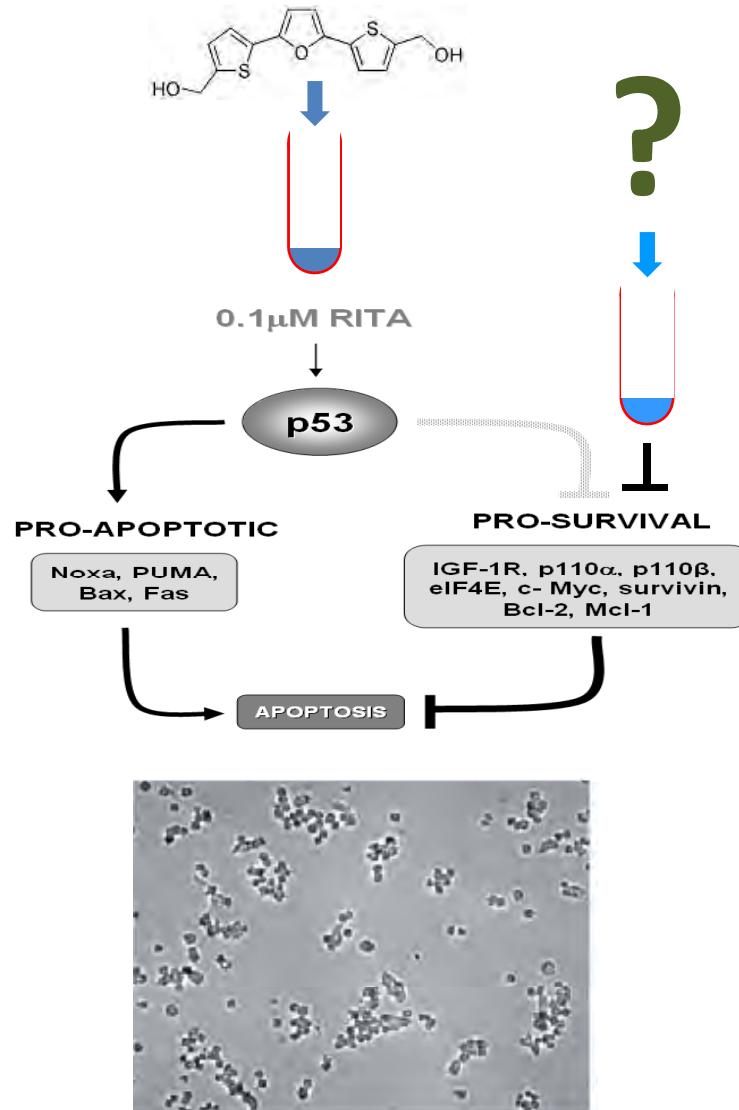
type: q22.12

from: 34700001

to: 36700000

siteID	Sequence name	type	from	to	length	properties
10578387	21	variation	35332780	35332781	2	
14340681	21	variation	35332776	35332781	6	
15319362	21	variation	35332764	35332764	1	
15319363	21	variation	35332766	35332766	1	
15319364	21	variation	35332768	35332768	1	
15319365	21	variation	35332770	35332770	1	
15319366	21	variation	35332772	35332772	1	

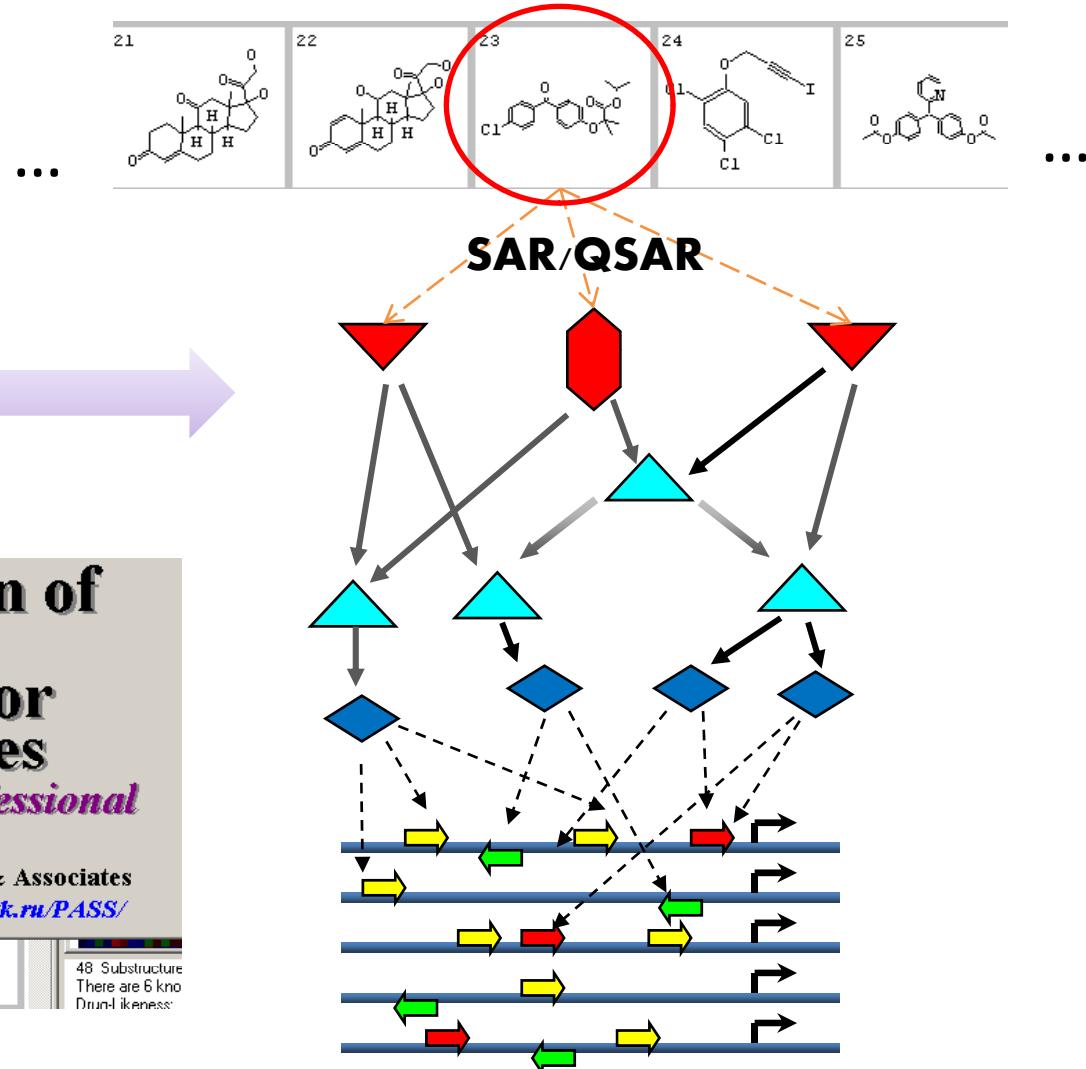
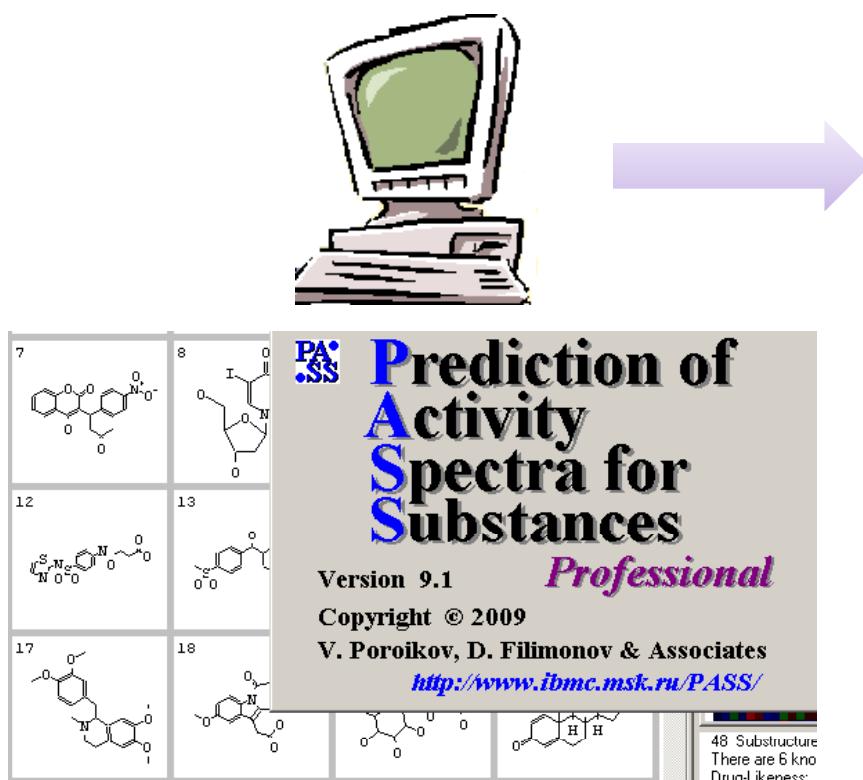
Apoptosis versus survival of cancer cells



07/09/2011

ChemNavigator Library
24 million
compounds

Identified
64 novel compounds



Tested 16 compounds in a panel of several cancer cell lines.

Found active:

Hypoxia inducible factor 1 alpha

Showed growth suppression.
The effect appears to be specific to cancer cells) and it did not affect normal mammary epithelial cells.

Found active:

Cyclin-dependent kinase 2 inhibitor

Out of panel of 7 different compounds without any effects in transformed mammary epithelial cells.



Scope: Format: Amount: GEO accession: **Series GSE11440**[Query DataSets for GSE11440](#)

Status

Public on Sep 08, 2008

Title

Role of Caveolin 1, E-Cadherin, Enolase 2 and PKCa on resistance to methotrexate in human HT29 colon cancer cells

Organism

[Homo sapiens](#)

Experiment type

Expression profiling by array

Summary

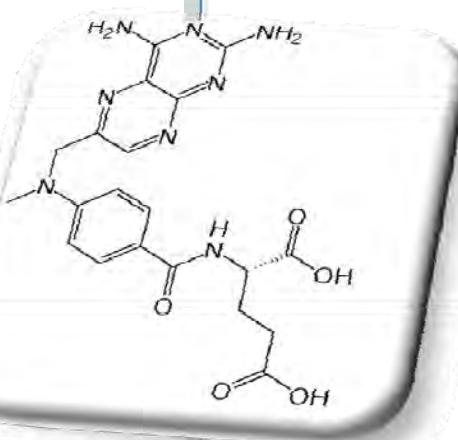
A summary of the work associated to these microarrays is the following:

Methotrexate (MTX) is one of the earliest cytotoxic drugs used in cancer therapy, and despite the isolation of multiple other folate antagonists, methotrexate maintains its significant role as a treatment for different types of cancer and other disorders. The usefulness of treatment with methotrexate is limited by the development of drug resistance, which may be acquired through different ways. To get insights into the mechanisms associated with drug resistance and sensitization we have performed a functional analysis of genes deregulated in methotrexate resistant cells, either due to its co-amplification with the DHFR gene or as a result of a transcriptome screening using microarrays. Genes adjacent to dhfr locus and included in the 5q14 amplicon were overexpressed in HT29 MTX-resistant cells. Treatment with siRNAs against those genes caused a slight reduction in cell viability in both HT29 sensitive and resistant cells. On the other hand, microarray analysis of HT29 and HT29 MTX resistant cells unveiled overexpression of caveolin 1, enolase 2 and PKCa genes in treated cells without concomitant copy number gain. siRNAs against these three genes effectively reduced cell viability and caused a decreased MTX resistance capacity. Moreover, overexpression of E-cadherin, which was found underexpressed in MTX-resistant cells, also sensitized the cells toward the chemotherapeutic agent. We provide functional evidences indicating that caveolin 1 and E-cadherin may play a critical role in cell survival and may constitute potential targets for coadjuvant therapy.

Keywords: DHFR, Methotrexate, drug resistance

Overall design

Two cell lines are compared in the study, which are HT29 colon cancer cells sensitive to methotrexate and HT29 cells resistant to 10e-5M MTX. Six



Contributor(s) [Selga E, Morales C, Noé V, Peinado MA, Ciudad CJ](#)
Citation(s)
Selga E, Morales C, Noé V, Peinado MA et al. Role of caveolin 1, E-cadherin, Enolase 2 and PKCalpha on resistance to methotrexate in human HT29 colon cancer cells. *BMC Med Genomics* 2008 Aug 11;1:35. PMID: [18694510](#)
Selga E, Oleaga C, Ramírez S, de Almagro MC et al. Networking of differentially expressed genes in human cancer cells resistant to methotrexate. *Genome Med* 2009 Sep 4;1(9):83. PMID: [19732436](#)

Submission date May 14, 2008
Last update date Jul 14, 2011
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Lab school of pharmacy
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City barcelona
State/province barcelona
ZIP/Postal code 08028
Country Spain

Platforms (1) [GPL570 \[HG-U133_Plus_2\] Affymetrix Human Genome U133 Plus 2.0 Array](#)

Samples (6)
[Less...](#)
[GSM288491](#) HT29 sensitive cells replicate 1
[GSM288497](#) HT29 sensitive cells replicate 2
[GSM288499](#) HT29 sensitive cells replicate 3
[GSM288501](#) HT29 resistant cells replicate 1
[GSM288502](#) HT29 resistant cells replicate 2
[GSM288536](#) HT29 resistant cells replicate 3

This SubSeries is part of SuperSeries:

[GSE16648](#) Networking of differentially expressed genes in human cancer cell lines resistant to methotrexate

Relations

Affiliated with [GSE28547 \(miRNA data\)](#)

RelationsAffiliated with [GSE28547 \(miRNA data\)](#)**Download family**[SOFT formatted family file\(s\)](#)**Format**[SOFT](#)[MINiML formatted family file\(s\)](#)[MINiML](#)[Series Matrix File\(s\)](#)[TXT](#)

Supplementary file	Size	Download	File type/resource
GSE11440_RAW.tar	47.5 Mb	(ftp) (http)	TAR (of CEL)

Raw data provided as supplementary file

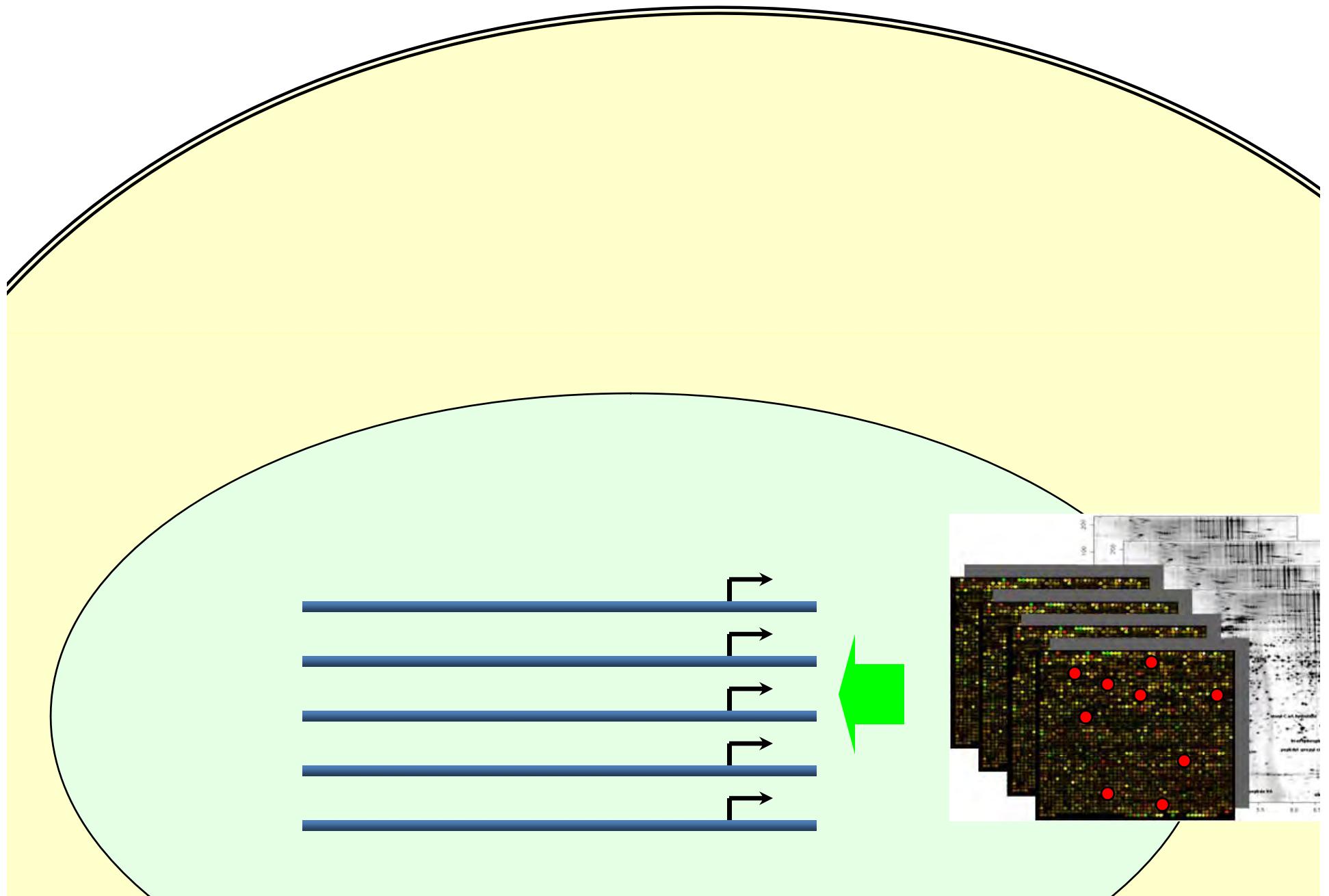
Processed data included within Sample table

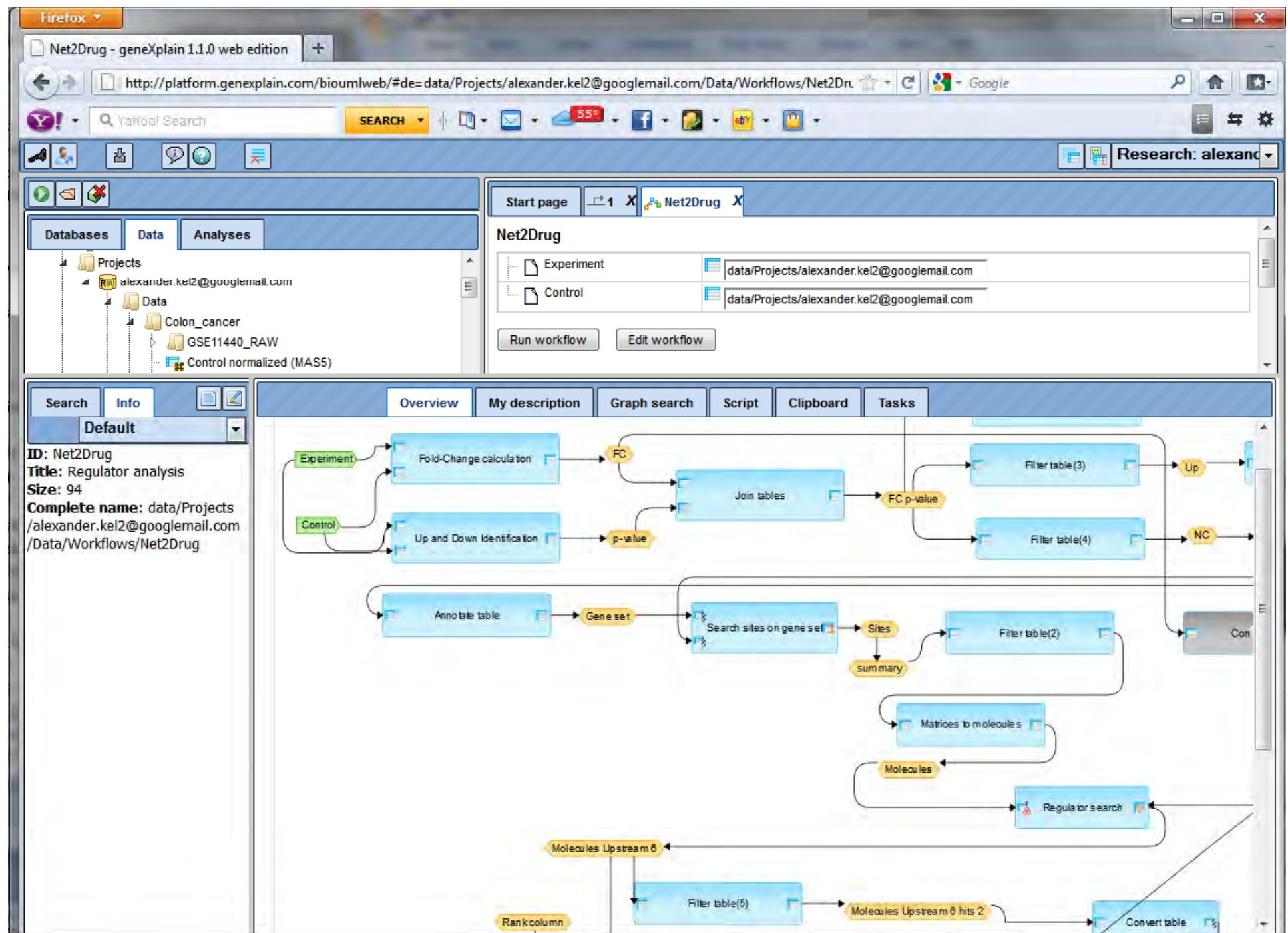
The screenshot shows the BioNumerics software interface. The top menu bar includes icons for file operations and a user profile labeled "Research: alexander". The left sidebar contains navigation tabs for "Databases", "Data", and "Analyses", and a tree view of project structure under "data". The main workspace displays a configuration dialog titled "Normalize Affymetrix exp... X". This dialog lists various parameters with dropdown menus or input fields:

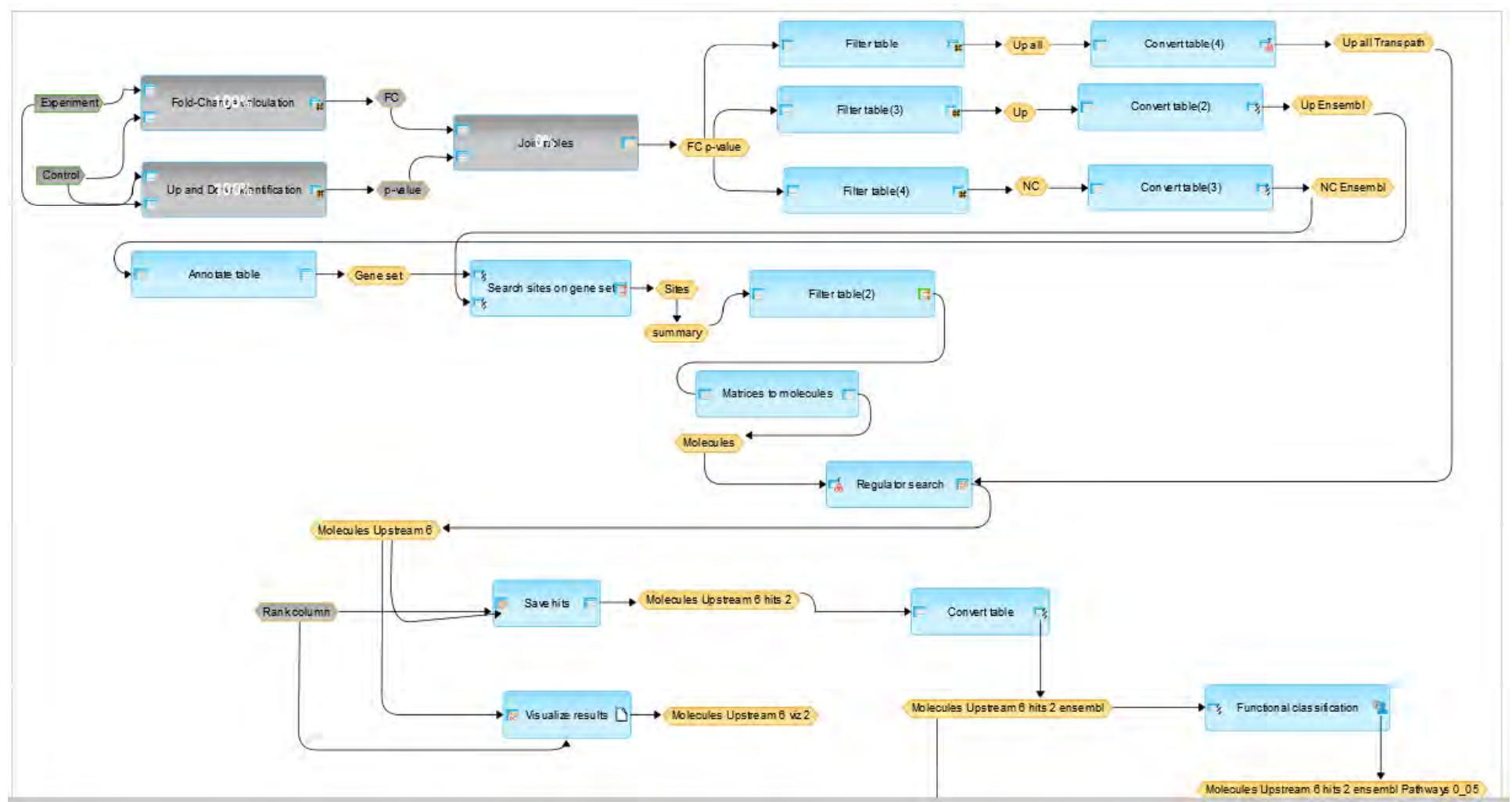
Experiment files	[3] GSM288501.CEL;GSM288502.CEL;GSM288536.CEL
Control files	[3] GSM288491.CEL;GSM288497.CEL;GSM288499.CEL
Method	MAS5
Background correction	MAS
Normalization method	quantiles
PM correction	pmonly
Summarization	mas
CDF version	(select element)
Output table test data	# .../Colon_cancer/Experiment normalized (MAS5) Auto
Output table control data	# .../ata/Colon_cancer/Control normalized (MAS5) Auto

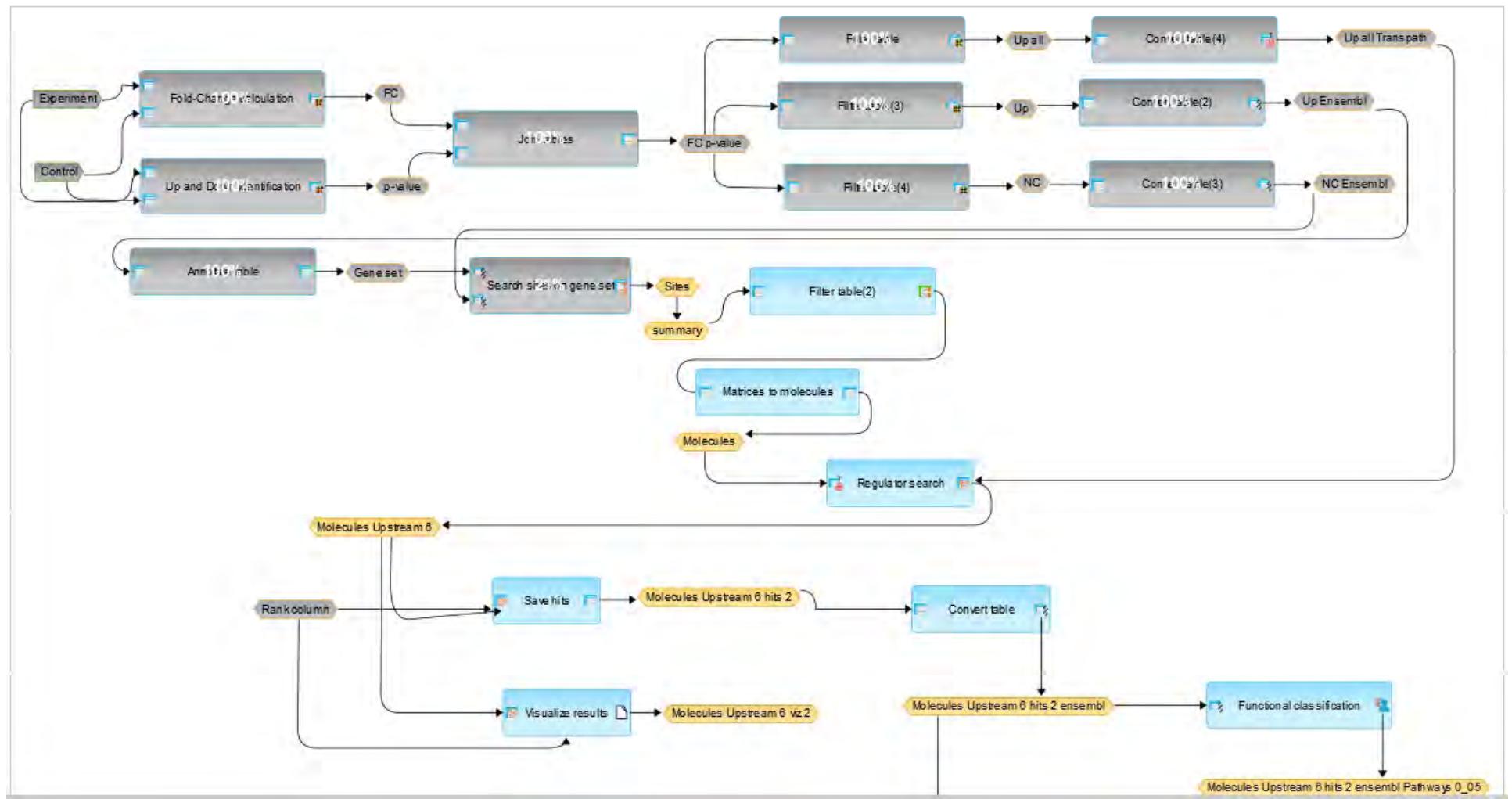
Below the dialog is a progress bar at 3% completion. A log window at the bottom shows the following informational messages:

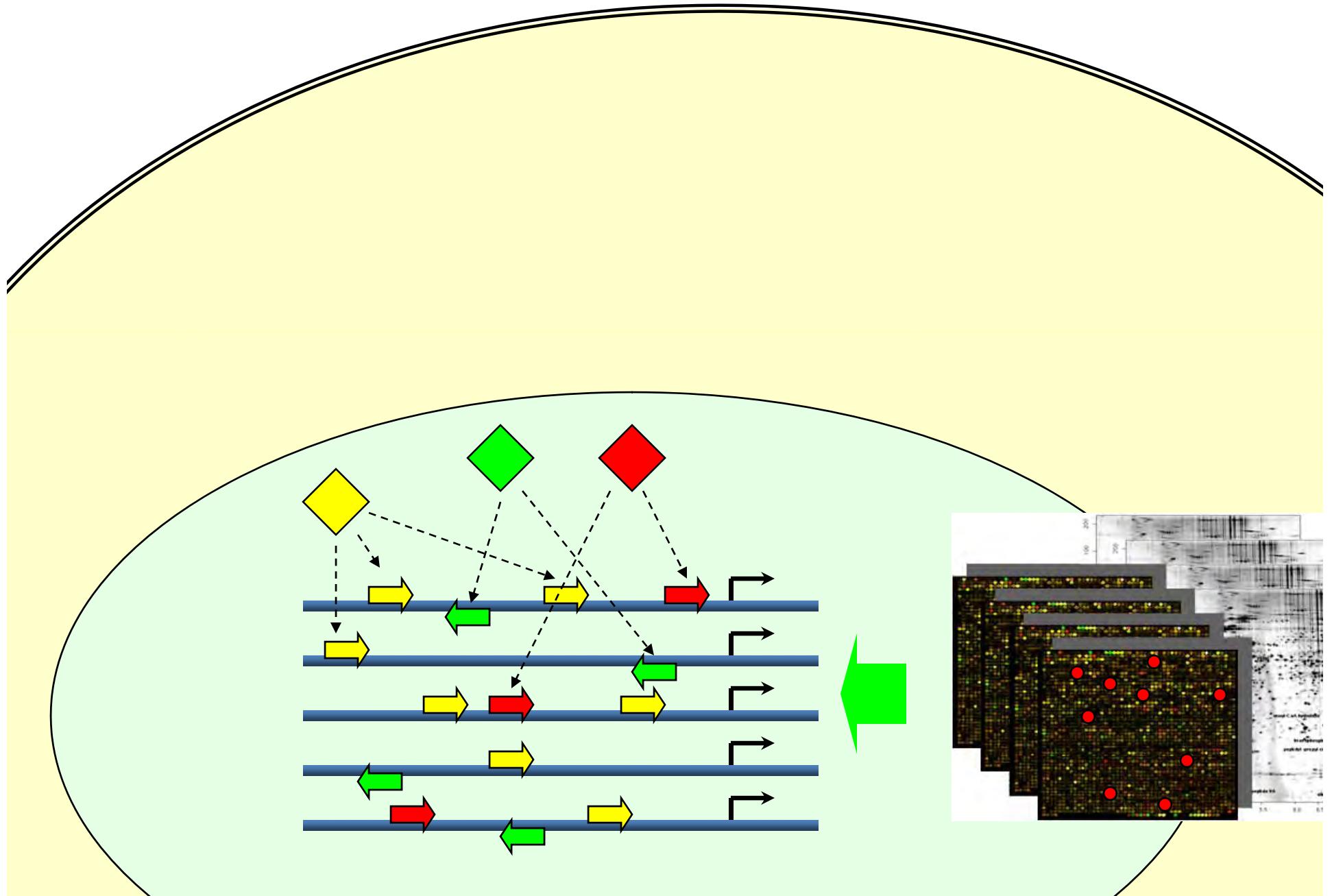
```
INFO - Normalize files...
INFO - Generating R command...
INFO - Platform detected: HG-U133_Plus_2
INFO - Connecting to R...
INFO - Invoking R command (that will take some time)...
```











Start page Molecules Upstream 6 PA... Experiment normalized (... X

ID	Yes density per 1000bp	No density per 1000bp	Yes-no ratio	Matrix cutoff	P-value
V\$CDPCR3_01	0.11552	0.01724	6.70061	0.8716	0.00428
V\$NIKX3A_01	0.24755	0.04023	6.15362	0.9372	3.7523E-5
V\$STAT_Q6	0.19804	0.03448	5.74338	0.9909	3.2222E-4
V\$PPARA_02	0.28055	0.0862	3.25458	0.8253	8.984E-4
V\$KAISO_01	0.19804	0.06321	3.13275	0.9929	0.00618
V\$PAX2_01	0.21454	0.07471	2.87169	0.8644	0.00701
V\$OCT1_07	0.39607	0.15516	2.55261	0.8629	8.7635E-4
V\$SREBP_Q3	0.5281	0.22987	2.29735	0.9162	4.7791E-4
V\$CMAF_01	1.18822	0.74708	1.59047	0.8444	0.00129
V\$AR_Q2	0.95717	0.61491	1.55662	0.777	0.005
V\$GATA4_Q3	1.6668	1.10338	1.51063	0.8533	6.3511E-4
V\$TST1_01	4.60434	3.64922	1.26173	0.8217	8.0258E-4
V\$TAL1BETAE47_01	3.8617	3.09178	1.24902	0.7841	0.00286
V\$XF2D_01	4.71986	3.86759	1.22036	0.7827	0.00296
V\$NCX_01	4.3733	3.59175	1.2176	0.8539	0.00443
V\$CEBPGAMMA_Q6	4.96741	4.13769	1.20053	0.7778	0.00467
V\$PAX4_03	5.84207	4.95949	1.17796	0.8931	0.00558
V\$HMGFIY_Q6	11.25505	9.93621	1.13273	0.8558	0.00335
V\$PAX2_02	16.05743	14.40147	1.11499	0.963	0.00224
V\$PAX6_01	18.38436	16.51629	1.1131	0.6045	0.00136
V\$DBP_Q6	17.79025	16.26918	1.09349	0.8364	0.00685

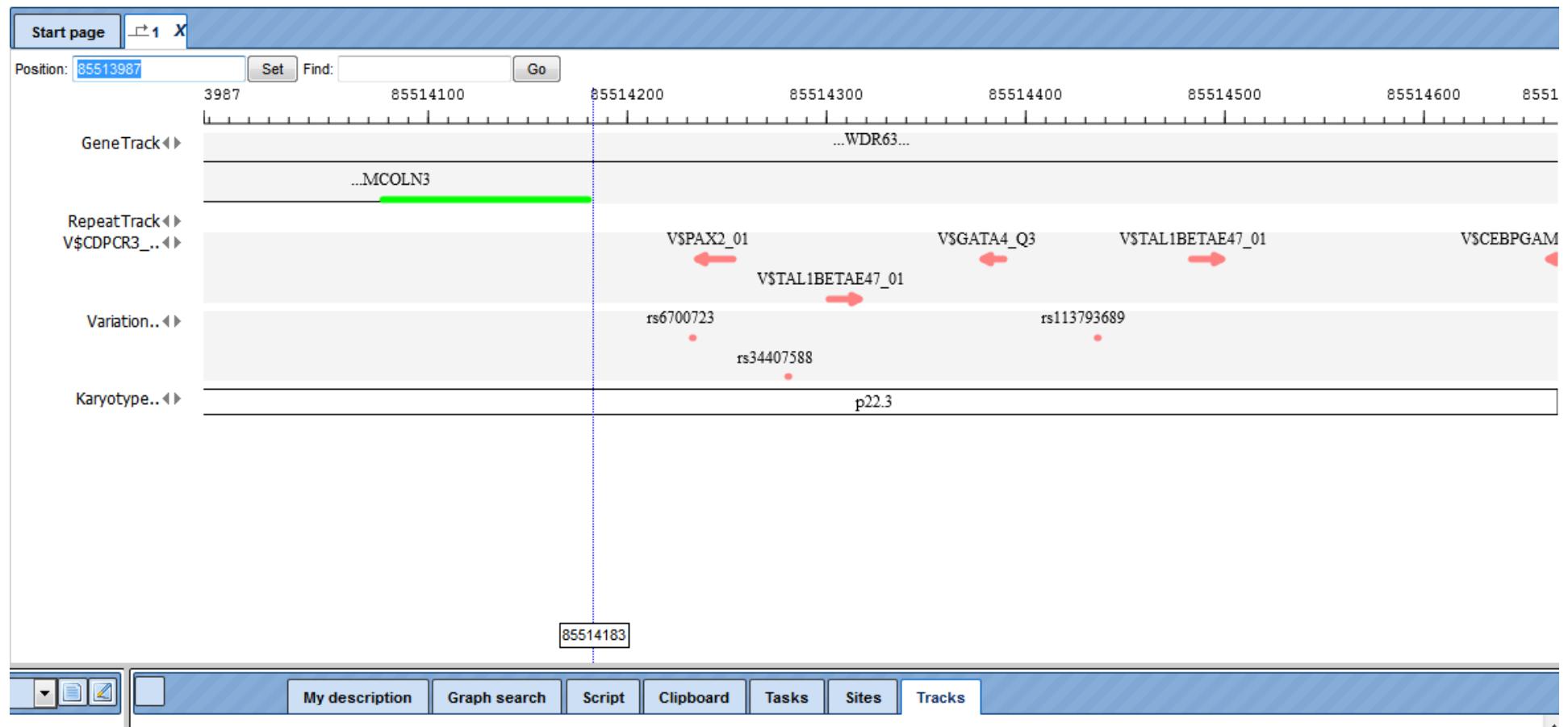
Search Info Default

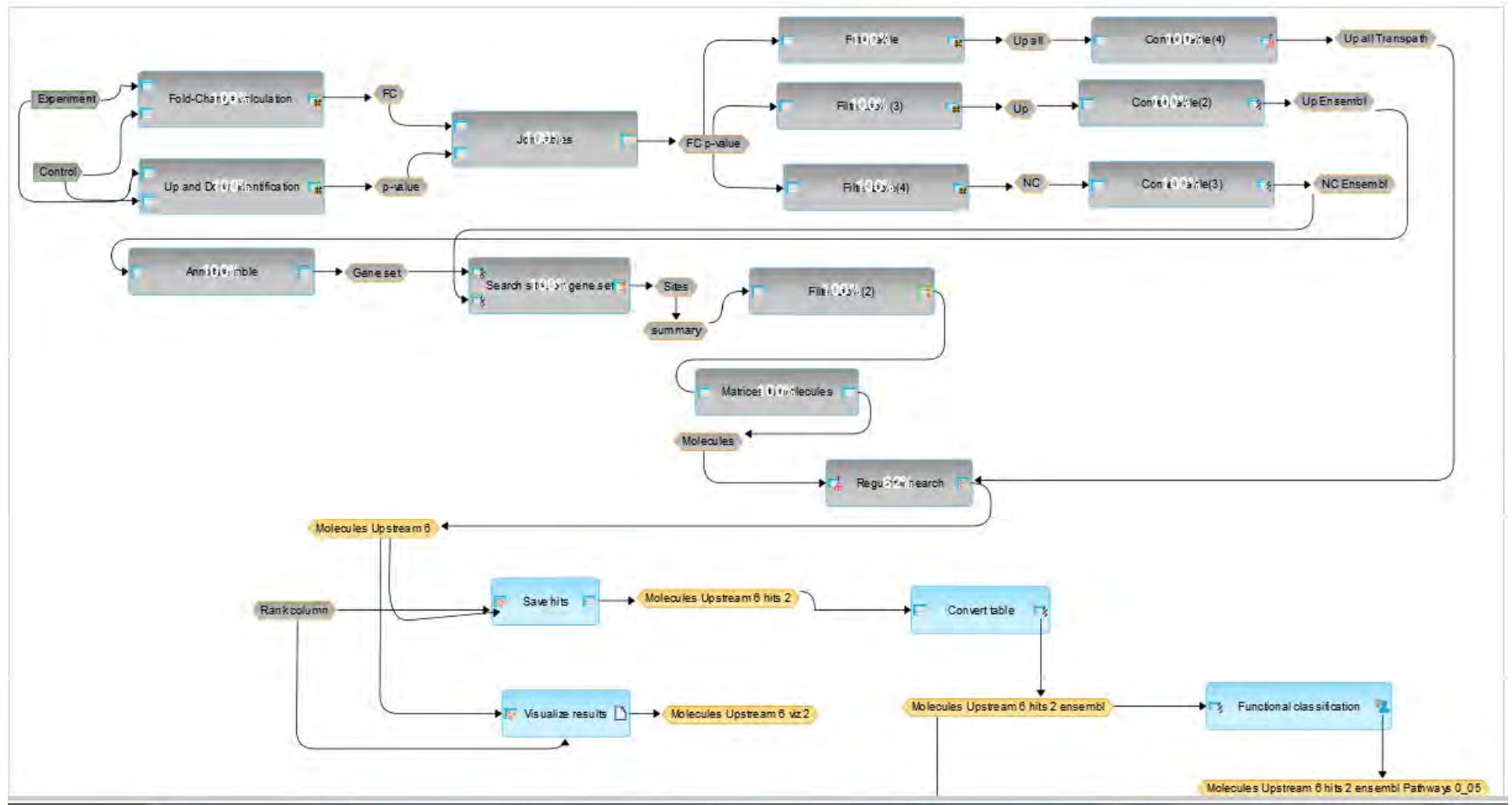
ID: summary
Size: 21
Complete name: data/Projects/alexander.kel2@googlemail.com/Data/Colon_cancer /Experiment normalized (MASS) FC p-value UP annotated_sites -500..100/summary

Template to construct the filtering expression:
- Select template -

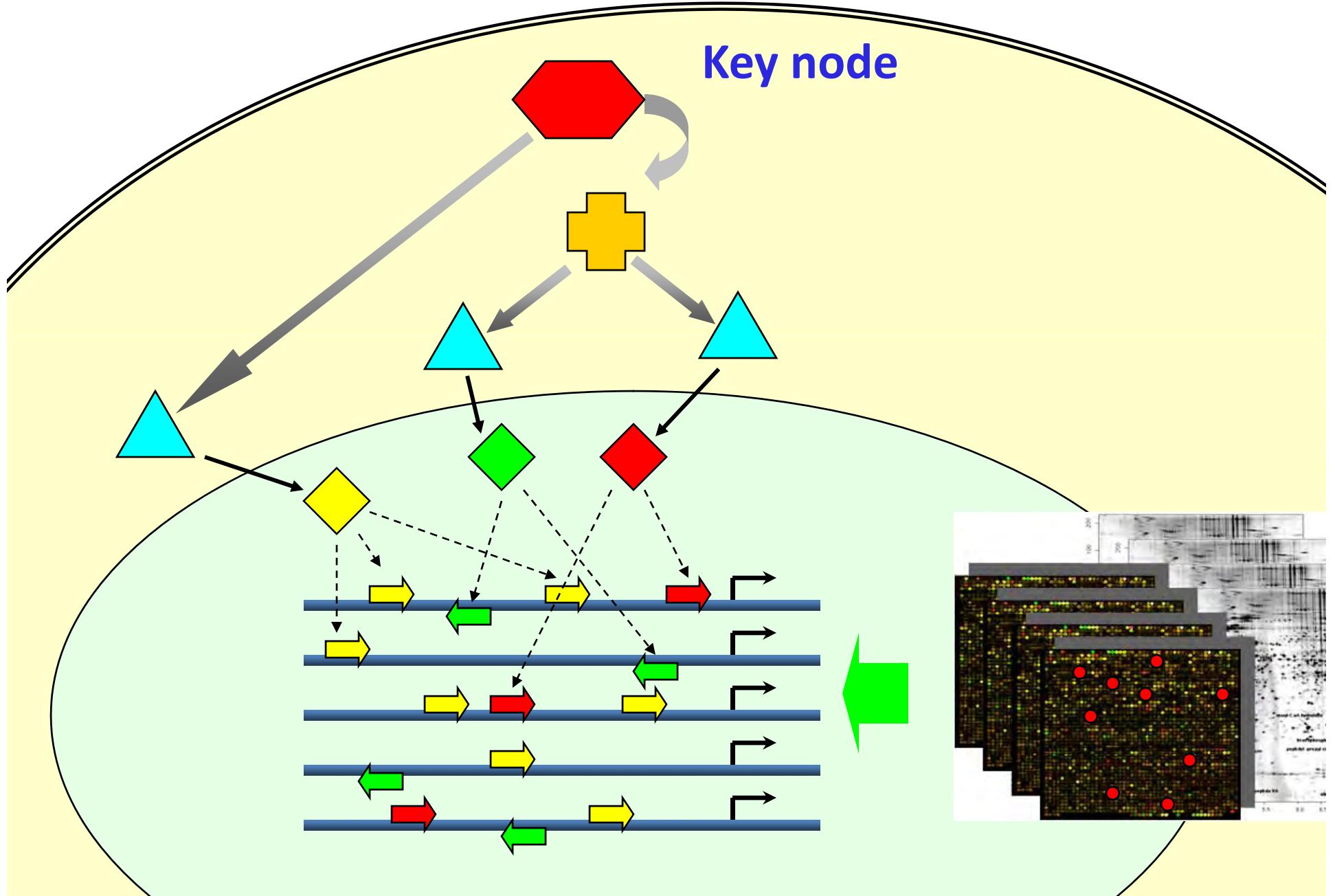
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ID
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No_density_per_1000bp
Yes_no_ratio
Matrix_cutoff
P_value

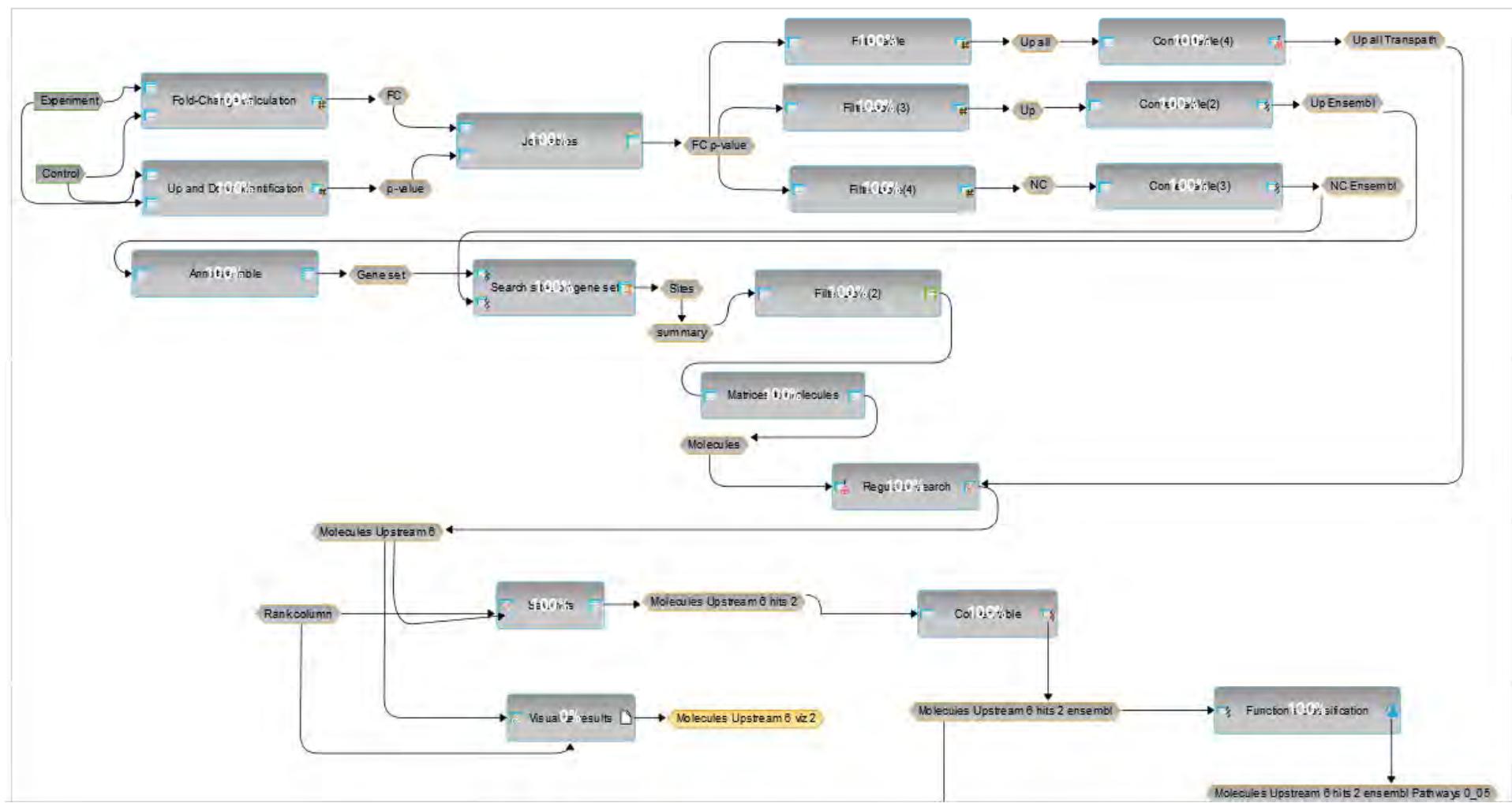
Expression in JavaScript language:





Key node





Research: Sysco

Databases Data Analyses

Stage I
Stage II
Stage III
CH000004420
site
Stage II FC
Stage II FC p-value
Stage II FC p-value Dn
Stage II FC p-value Dn genes
Stage II FC p-value Dn genes annotated
Stage II FC p-value Dn genes GO (biological)
Stage II FC p-value Dn genes GO (biological) n
Stage II FC p-value Dn genes Promoters
Stage II FC p-value Dn genes sites -2000..500
Stage II FC p-value Dn genes sites -500..100
Stage II FC p-value Dn lipid metabolic process
Stage II FC p-value Dn lipid metabolic process
Stage II FC p-value Dn Sites
ENSG00000117054
ENSG00000136872

Molecules filtered X Molecules filtered Upstre... X Molecules filtered Upstre... X

Search Info Overview My description Graph search Script Clipboard SQL Editor Tasks

Default

ID: Regulator analysis
Title: Regulator analysis
Size: 58
Complete name:
data/Projects/Project3
/Data/Workflows
/Regulator analysis

Gene set

Annotate table

Set annotated

Background set

Filter table

Gene set filtered

Search sites on gene set

Sites

summary

Convertible(2)

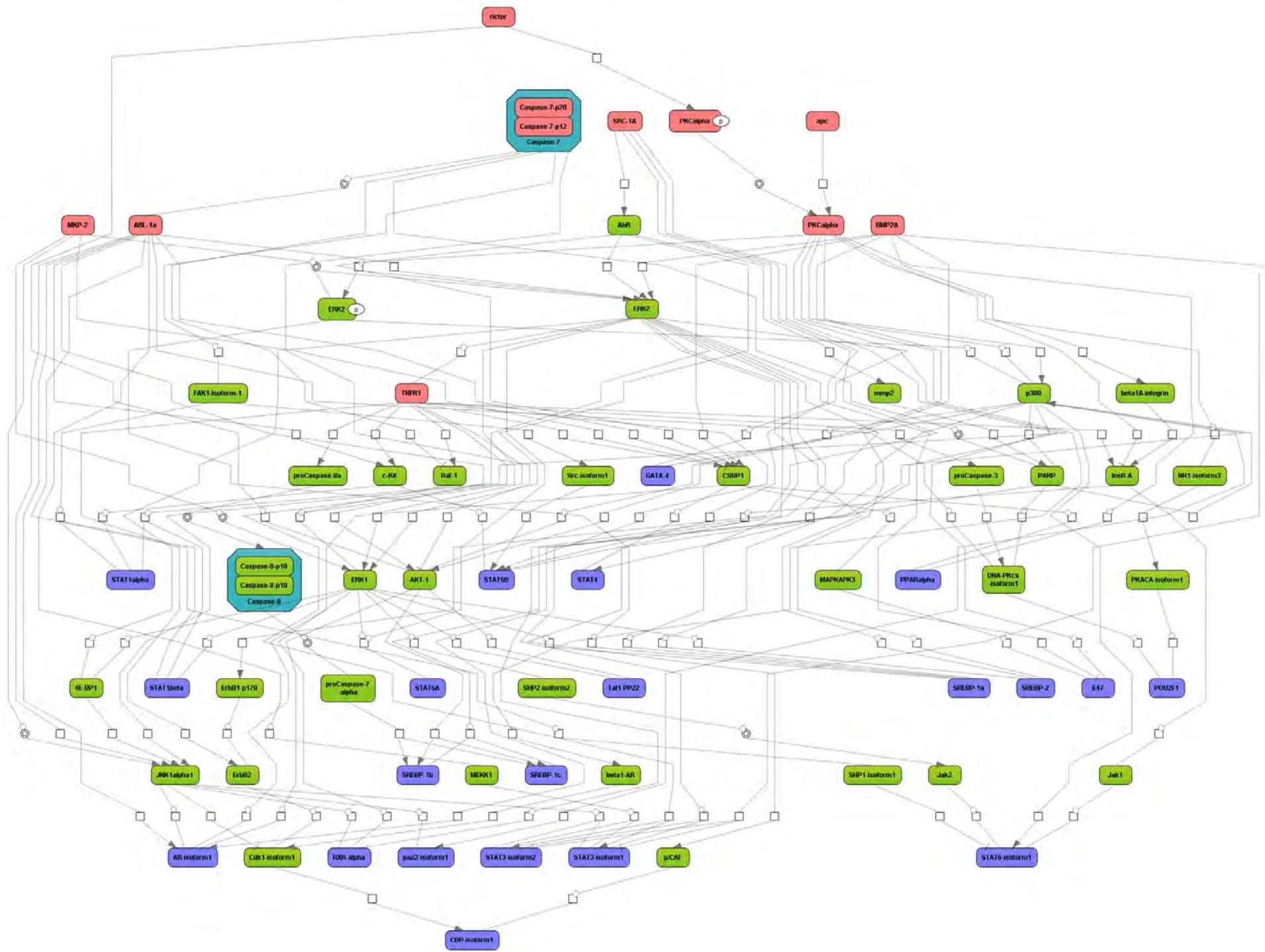
Matrices to molecules

Molecules

Regulator search

GenesetTranspath

Regulator search



Start page Molecules Upstream 6 PA... X

ID	Hits names	Master molecule name	Reachable total	Reached from set	Score	Description	Molecule type	PASS activity
MO000107848	AR-isoform1(h), CDP-isoform1(h), E47(h), GATA-4(h), POU2F1(h), ...	Cdk1-isoform2(h)	21317	21	0.58876	cell division cycle 2, G1 to S and G2 to M	basic	Cyclin-dependent kinase 1 inhibitor; Cyclin-dependent kinase inhibitor
MO000023154	AR-isoform1(h), CDP-isoform1(h), E47(h), GATA-4(h), POU2F1(h), ...	PKCbeta2(h)	16078	21	0.45328	protein kinase C, beta	basic	Protein kinase C inhibitor; Protein kinase C stimulant
MO000082228	AR-isoform1(h), CDP-isoform1(h), E47(h), GATA-4(h), POU2F1(h), ...	ErbB1-p60(h)	13125	18	0.29716	epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog, avian)	basic	Epidermal growth factor antagonist; Epidermal growth factor receptor kinase inhibitor; ErbB-1 antagonist
MO000082230	AR-isoform1(h), CDP-isoform1(h), E47(h), GATA-4(h), POU2F1(h), ...	ErbB1-p110(h)	13125	18	0.29716	epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog, avian)	basic	Epidermal growth factor antagonist; Epidermal growth factor receptor kinase inhibitor; ErbB-1 antagonist
MO000087397	AR-isoform1(h), CDP-isoform1(h), E47(h),	ErbB1-4(h)	13125	18	0.29716	epidermal growth factor receptor (erythroblastic leukemia viral	basic	Epidermal growth factor antagonist; Epidermal growth factor

Search Info Default Filters Columns My description Graph search Script Clipboard Tasks

ID: Molecules Upstream 6 PASS activity filtered 3 hits
Size: 9

Template to construct the filtering expression: Columns (double-click to paste):

PASS / PharmaExpert multi-target search

Multitargeted actions

Effects: Vascular (peripheral) disease treatment Number of targets: 4 Run Save

Cyclin-dependent kinase 1 inhibitor
Epidermal growth factor antagonist
Interferon agonist
MAP kinase inhibitor
Protein kinase C inhibitor

No	Pa	Number	Activity type	Activity type	Activity type
1	0.371	9	Cyclin-dependent kinase 1 inhibitor	Epidermal growth factor antagonist	
2	0.534	4	Cyclin-dependent kinase 1 inhibitor	Interferon agonist	
3	0.295	4	Cyclin-dependent kinase 1 inhibitor	MAP kinase inhibitor	
4	0.534	2	Epidermal growth factor antagonist	Interferon agonist	
5	0.110	5	Epidermal growth factor antagonist	MAP kinase inhibitor	
6	0.182	3	Interferon agonist	MAP kinase inhibitor	
7	0.534	2	Cyclin-dependent kinase 1 inhibitor	Epidermal growth factor antagonist	Interferon agonist
8	0.103	3	Cyclin-dependent kinase 1 inhibitor	Epidermal growth factor antagonist	MAP kinase inhibitor
9	0.100	1	Cyclin-dependent kinase 1 inhibitor	Interferon agonist	MAP kinase inhibitor
10	0.100	1	Epidermal growth factor antagonist	Interferon agonist	MAP kinase inhibitor
11	0.100	1	Cyclin-dependent kinase 1 inhibitor	Epidermal growth factor antagonist	Interferon agonist

PASS / PharmaExpert – imiquimod

Prediction & Interpretation - C:\KEL\PASS\prestwick_chemical_library_cured-antineoplastic0.5.sdf. 98/108

The screenshot displays the PASS / PharmaExpert software interface. At the top, several chemical structures are shown: Flunixin meglumine, Acitretin, Cortisone, 2-Chloropyrazine, Equulin, Imiquimod (highlighted in blue), and Clotrimazole. Below these, a search bar allows filtering by chemical name, with 'Pa' and 'Pi' dropdowns and a 'Sort' button. The main list shows various activities with their Pa and Pi values. A detailed list of predicted effects for imiquimod is shown on the right, categorized by mechanism. The bottom section contains a table of additional activities and a toolbar with buttons for Delete, Clear, Load, Include, and Save.

Activity	Pa	Pi
Homoserine dehydrogenase inhibitor	0.137	0.122
2-Amino-4-hydroxy-6-hydroxymethylhydropteridine diphosphokinase inhibitor	0.044	0.030
Purinergic P2Y1 antagonist	0.042	0.028
Inositol 1,4,5-triphosphate receptor antagonist	0.077	0.063
Growth hormone antagonist	0.234	0.220
NMN nucleosidase inhibitor	0.062	0.048
Phosphatidylcholine-retinol O-acyltransferase inhibitor	0.263	0.250
Antimyopathies	0.262	0.249
Histamine release inhibitor	0.226	0.213
D-Octopine dehydrogenase inhibitor	0.113	0.100
Antimycobacterial	0.194	0.182
Cysteine-tRNA ligase inhibitor	0.075	0.063
Glycerol dehydrogenase inhibitor	0.078	0.066
Retinal oxidase inhibitor	0.309	0.297
Nardilysin inhibitor	0.171	0.160
D-lactate dehydrogenase inhibitor	0.116	0.105
Constipation treatment	0.094	0.083
Glycine amidinotransferase inhibitor	0.173	0.162
Antiprotozoal (Trypanosoma)	0.205	0.195
CMP-N-acetylneuraminate monooxygenase inhibitor	0.095	0.085
Cyclin-dependent kinase 1 inhibitor	0.055	0.045
Transactivator transcription protein inhibitor	0.183	0.174
Substance inhibits cyclin-dependent kinase 1. EC 2.7.1.37.CDK		

Number of selected compounds: 2

<chemical_name> imiquimod; > <DRUG_LIKENESS> 0.952; 35 Substructure descriptors, 0 new; 672 Possible activities.



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Search



Imiquimod

From Wikipedia, the free encyclopedia

Imiquimod (INN) is a prescription medication that acts as an immune response modifier. It is marketed by MEDA AB, Graceway Pharmaceuticals and iNova Pharmaceuticals under the trade names **Aldara** and **Zyclara**, and by Mochida as **Beselna**.

Contents [hide]

- [1 History](#)
- [2 Uses](#)
- [3 Mechanism of action](#)
- [4 Disadvantages](#)
- [5 Chemistry](#)
- [6 See also](#)
- [7 References](#)
- [8 External links](#)

History

[\[edit\]](#)

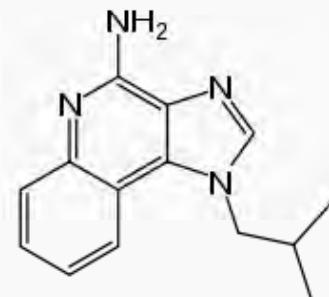
The original FDA approval was on February 27, 1997, FDA Application No. (NDA) 020723, by 3M. Imiquimod is approved to treat actinic keratosis, superficial basal cell carcinoma, and external genital warts. Adverse side effects have been reported, in some cases serious and systemic, resulting in the revision of warning labels.

Uses

[\[edit\]](#)

Imiquimod is a patient-applied cream used to treat certain diseases of the skin, including **skin cancers** (**basal cell carcinoma**, **Bowen's disease**,^[1] **superficial squamous cell carcinoma**, **some superficial malignant melanomas**, and **actinic keratosis**) as well as **genital warts** (**condylomata acuminata**). It has also been tested for treatment of **molluscum contagiosum**, **vulvar intraepithelial neoplasia**, **common warts** that have proven difficult to treat,^[2] and **vaginal intraepithelial neoplasia**.^[3] Outstanding cosmetic result has resulted from the treatment of both

Imiquimod



Systematic (IUPAC) name

3-(2-methylpropyl)-3,5,8-triazatricyclo[7.4.0.0^2,6]trideca-1(9),2(6),4,7,10,12-hexaen-7-amine

Clinical data

Licence data EMA:link, US FDA:link

Pregnancy B1(AU) C(US)
cat.

Legal status POM (UK) B-only (US)

Routes Topical

Pharmacokinetic data

Half-life 30 hours (topical dose), 2 hours (subcutaneous dose)

Identifiers

CAS number 99011-02-6

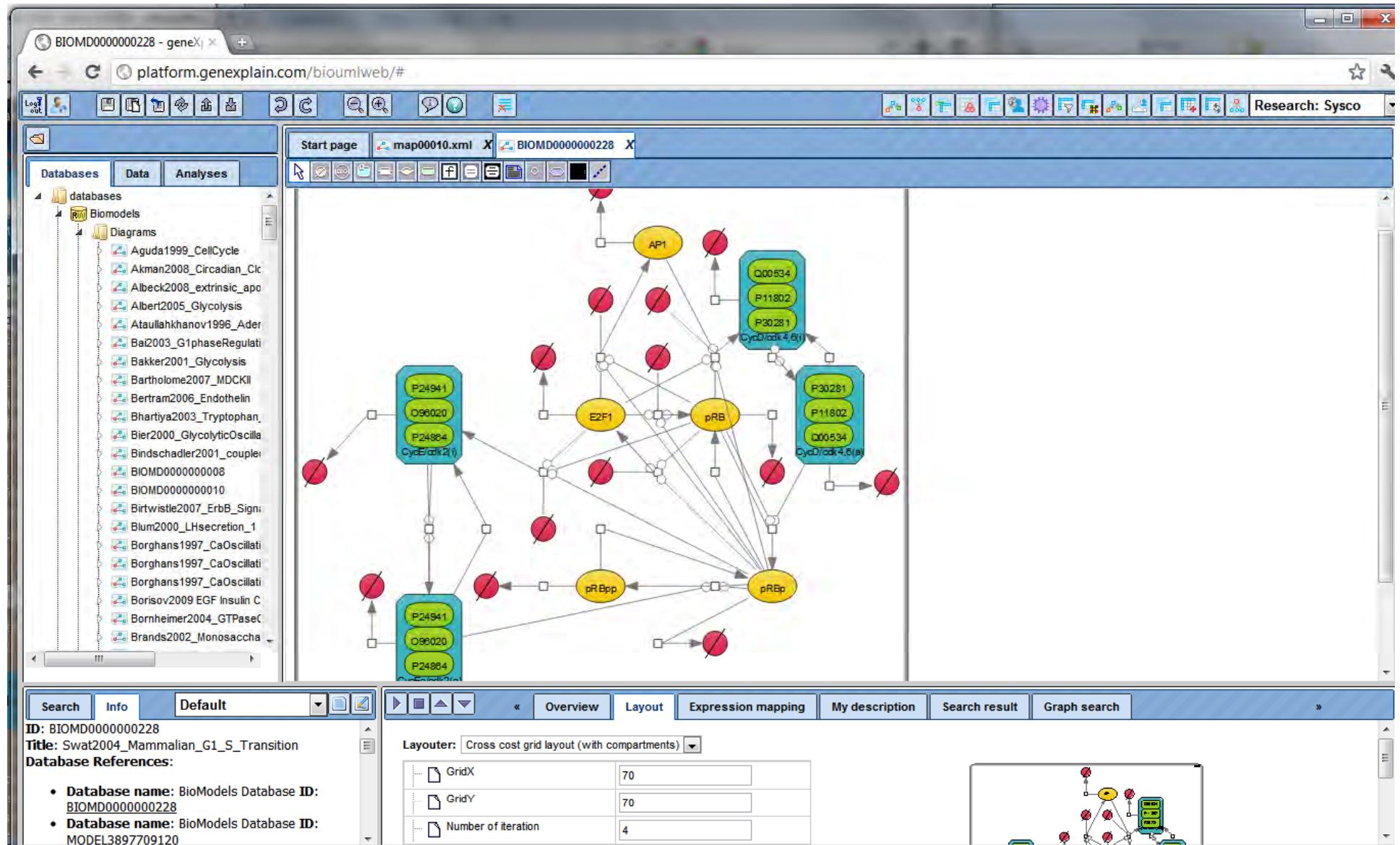
ATC code D06BB10

PubChem CID 57469

DrugBank DRUGBANK

BioUML: platform for collaborative research

- Cloud computing: Amazon EC2 servers
- data repository
 - groups,
 - projects,
 - import/export, FTP upload
- chat
 - community efforts
 - history (in process)



BIOMD0000000228 - geneX | platform.genexplain.com/bioumlweb/#

Databases Data Analyses

databases

- Biomodels
 - Diagrams
 - Aguda1999_CellCycle
 - Akman2008_Circadian_Clk
 - Albeck2008_extrinsic_apo
 - Albert2005_Glycolysis
 - Ataullahkhanov1996_Ader
 - Bai2003_G1phaseRegulati
 - Bakker2001_Glycolysis
 - Bartholome2007_MDCKII
 - Bertram2006_Endothelin
 - Bhartiya2003_Tryptophan
 - Bier2000_GlycolyticOscilla
 - Bindschadler2001_couple
 - BIOMD0000000008
 - BIOMD0000000010
 - Birtwistle2007_ErbB_Sign
 - Blum2000_LHsecretion_1
 - Borghans1997_CaOscillati
 - Borghans1997_CaOscillati
 - Borghans1997_CaOscillati

Start page map00010.xml BIOMD0000000228

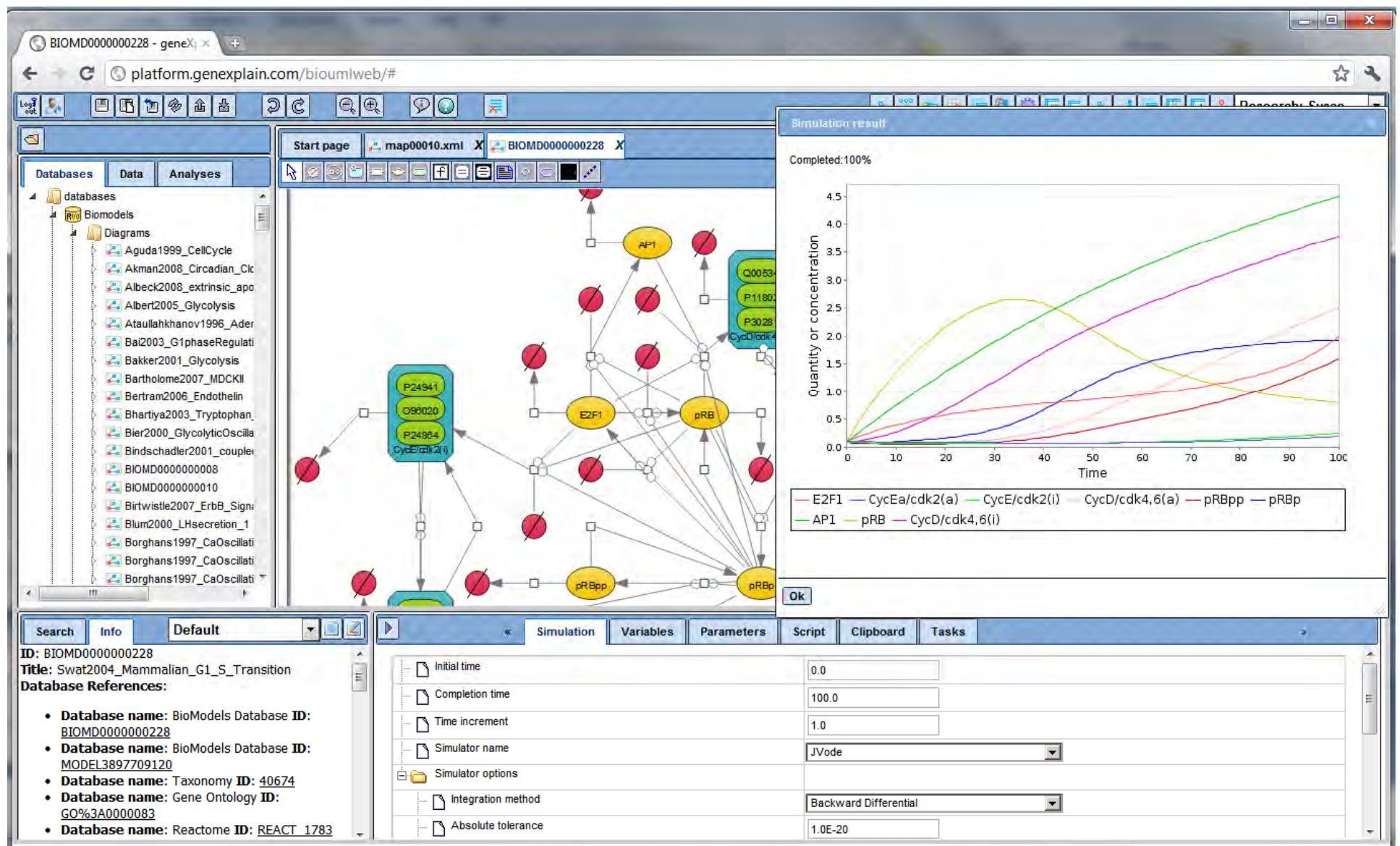
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 Title: Swat2004_Mammalian_G1_S_Transition
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- Database name: Taxonomy ID: 40674
- Database name: Gene Ontology ID: GO%3A0000083
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Simulation Variables Parameters Script Clipboard Tasks

Name	Initial value	Constant	Units	Show in plot	Plot line spec	Comment
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J11	0.5	<input checked="" type="checkbox"/>			-	J11
J12	5.0	<input checked="" type="checkbox"/>			-	J12
J13	0.0020	<input checked="" type="checkbox"/>			-	J13
J15	0.0010	<input checked="" type="checkbox"/>			-	J15



Firefox ▾

Acetate_utilization - BioUML 0.9.2 ... +

http://ie.biouml.org/bioumlweb/#de=databases/PantherDB/Diagrams/Acetate_utilization

Google

Databases Data Analyses Users

users

- Apoptosis
- Biomodels
- Cancer therapy
- GeneNet
- Genetics
- ISB
- LipidomicNet
- Net2Drug
- Group chat
- Expand/collapse
- kel
- net2drug
- shrus79
- vvp
- Sysco
- support
- anna
- ian
- tolstyh

Acetate utilization X

The diagram illustrates a metabolic pathway involving Acetate kinase, Acetyl-CoA synthetase, and Acetylphosphate. Reaction r1 shows Acetate kinase catalyzing the conversion of Acetate and ADP to Acetylphosphate and ATP. Reaction r2 shows Acetylphosphate being converted to Acetyl-CoA and AMP. Reaction r3 shows Acetyl-CoA synthetase catalyzing the conversion of Acetyl-CoA and ATP to Acetate and CoA.

Acetate kinase Acetate Acetyl-CoA synthetase

Acetylphosphate

r1 r2 r3

ATP ADP Acetate ATP CoA Acetyl-CoA AMP

ian@ie.biouml.org

User status: online

fedor@ie.biouml.org(16:43:14):
Hello,
ian@ie.biouml.org(16:43:23):
Hello
fedor@ie.biouml.org(16:43:25):
this is just a test for screenshot

Search Info Default

ID: Net2Drug
Size: 7
Complete name: users/Net2Drug

Send Close

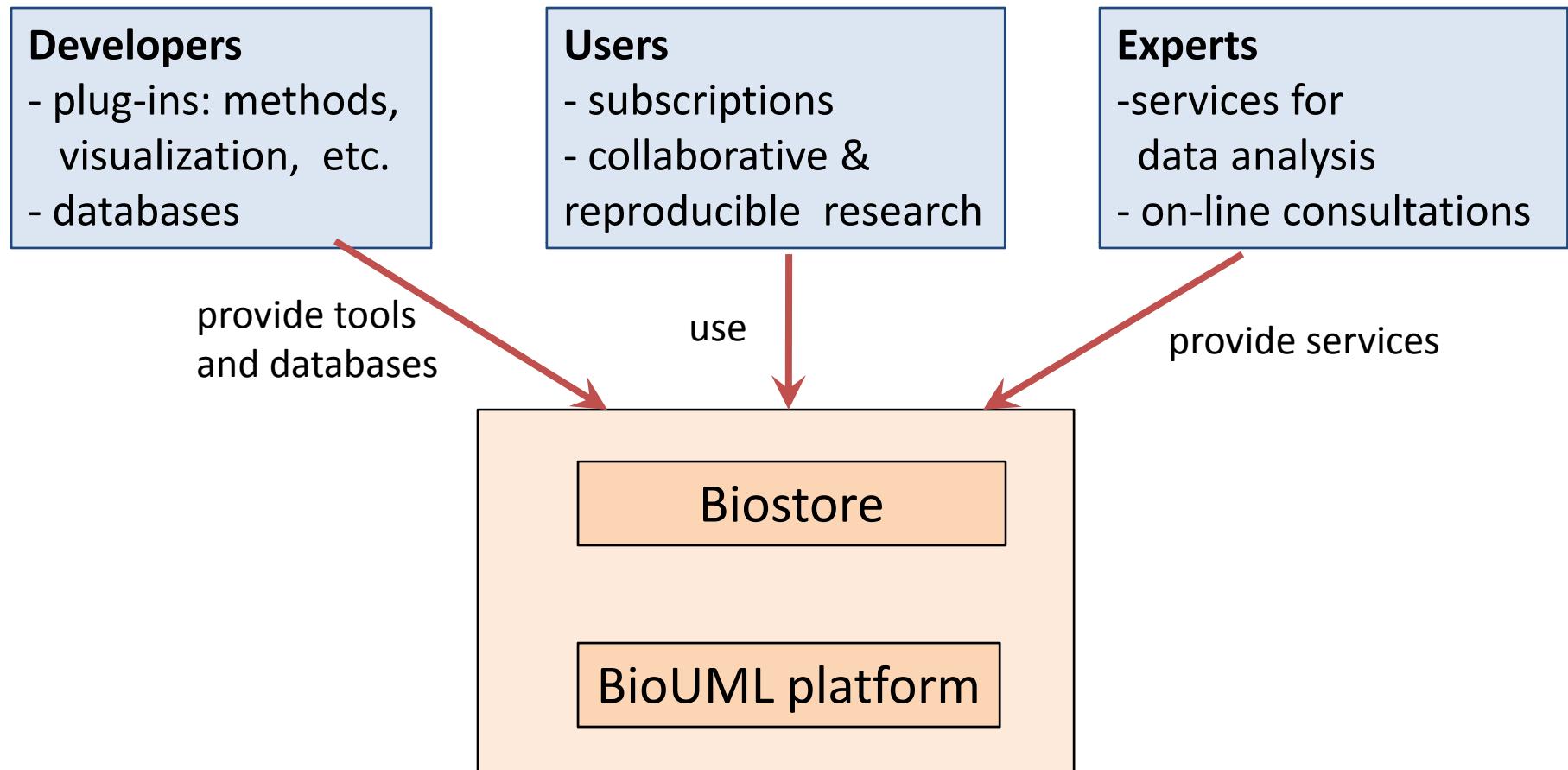
http://ie.biouml.org/bioumlweb/#

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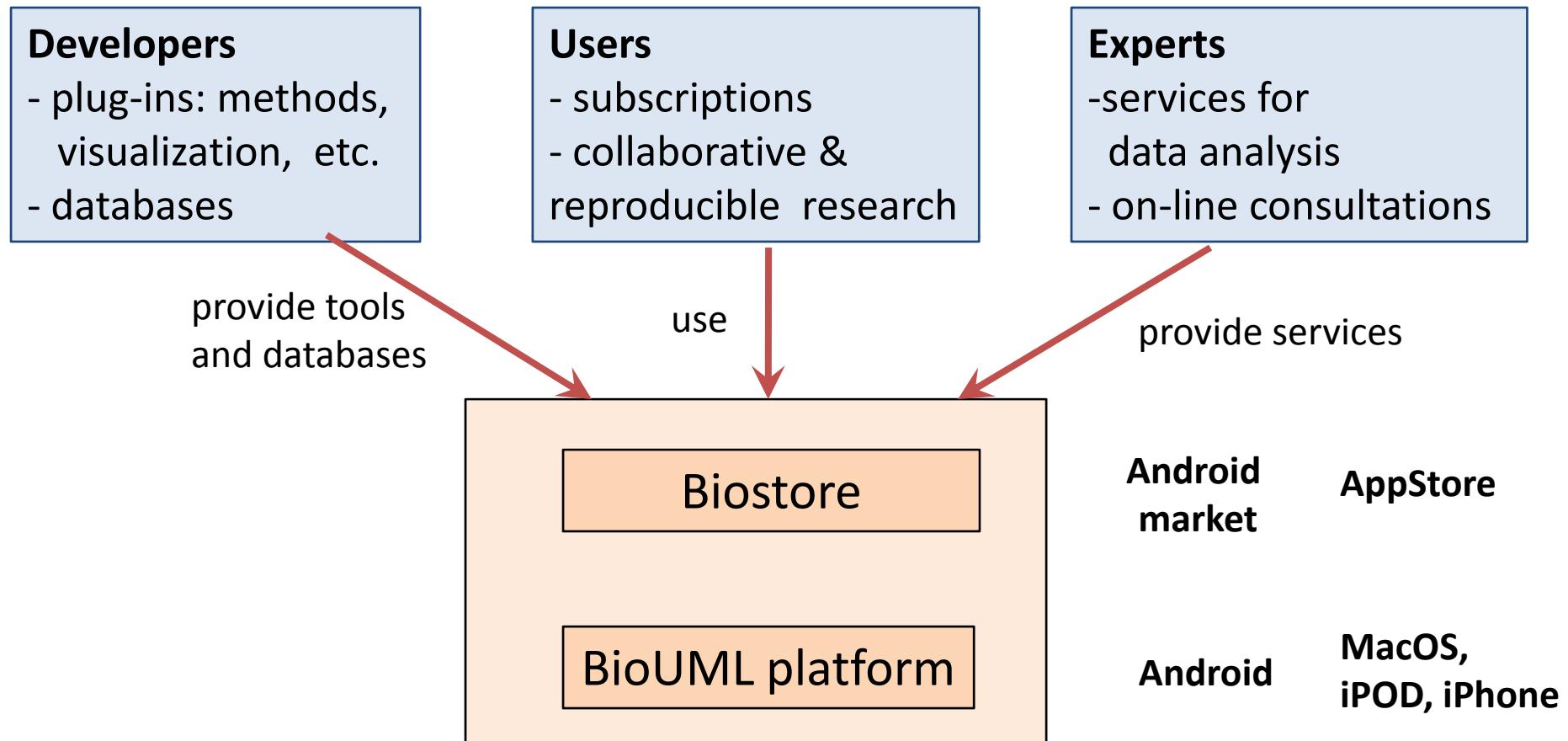
- Biostore
- LIMS

(Laboratory Information Management System)

BioUML ecosystem



The power of platform: Google and Apple as an examples



Google



geneXplain - Open Cosmos - BioUML

NGS

Drug Analysis
[QSAR, Drug targets]

Network Analysis
[GeneWays, Simulation,
Fitting]

Transcriptome Analysis
[R/Bioconductor, Meta-analysis]

Epigenome Analysis
[ChIP-seq, TF-sites, miRNA]

Genome Analysis
[Genome browser, Galaxy]

Acknowledgements

Part of this work was partially supported by the grant:
European Committee grant №037590 “**Net2Drug**”
European Committee grant №202272 “**LipidomicNet**”
Integration and interdisciplinary grants №16, 91 of SB RAS.

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