

Cell Signaling and Signaling Pathways

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September 30th, 2016



GDA

International Course on
Genomic Data Analysis



PRINCIPE FELIPE
CENTRO DE INVESTIGACION

Where are we?

Gene Expression Data Analysis

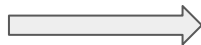
Functional Profiling: FatiGO and
Gene Set Analysis

Signaling Pathways Analysis



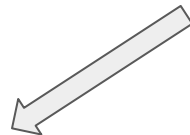
The results we obtained

Differential Expression of RNA-Seq



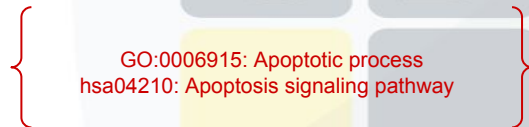
Genes with
 $p < 0.05^*$
*fold change > 2.0**
**thresholds defined by user*

Functional Profiling: FatiGO and
Gene Set Analysis



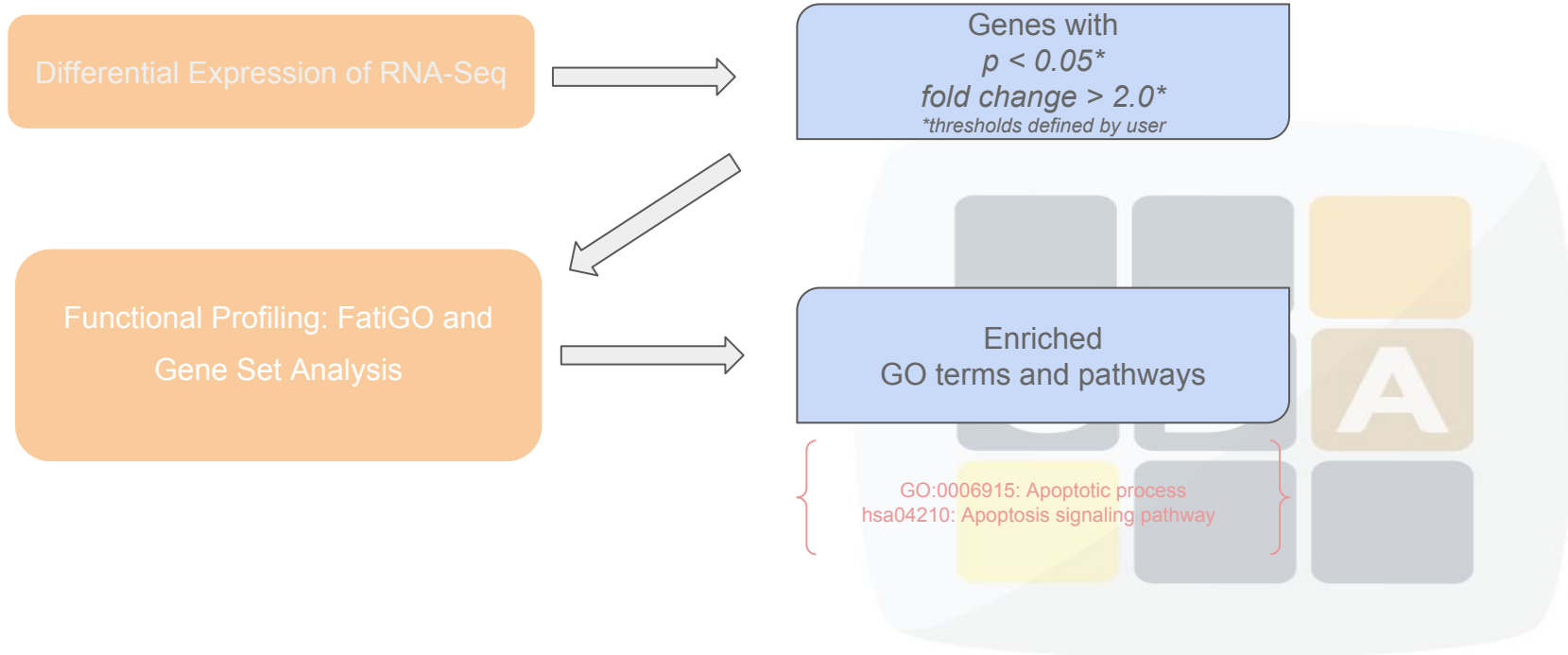
Enriched
GO terms and pathways

GO:0006915: Apoptotic process
hsa04210: Apoptosis signaling pathway



Do we have enough biological answer?

We want to understand cellular mechanisms of different phenotypes from their genotypes.

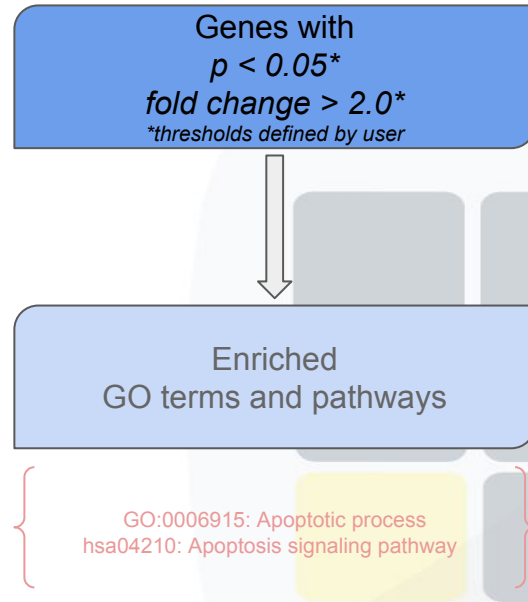


Do we have enough biological answer?

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Do the rest of the genes not contribute to pathogenesis of disease?

Is it enough to use only significant genes as biomarkers of multigenic disease?



Do we have enough biological answer?

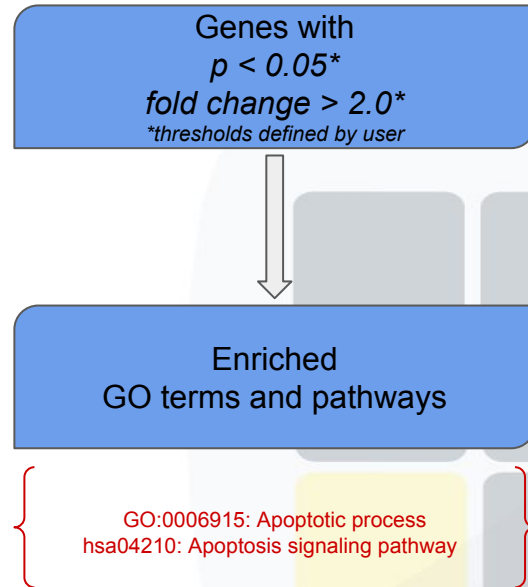
We want to understand cellular mechanisms of different phenotypes from their genotypes

Do the rest of the genes not contribute to pathogenesis of the disease?

Is it enough to use only significant genes as biomarkers of multigenic diseases?

In 2016, can the following conclusion be satisfactory?

Our analysis showed that apoptotic process and apoptosis signaling pathway is more significant in groupA....



Do we have enough biological answer?

We want to understand cellular mechanisms of different phenotypes from their genotypes

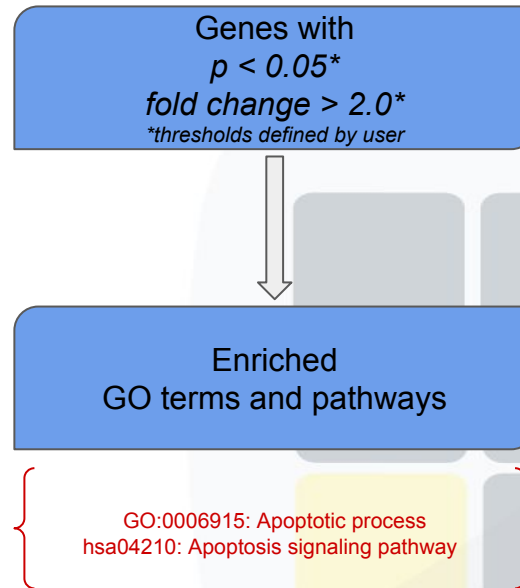
Do the rest of the genes not contribute to pathogenesis of the disease? **(NO)**

Is it enough to use only significant genes as biomarkers of multigenic diseases? **(NO)**

In 2016, can the following conclusion be satisfactory?

Our analysis showed that apoptotic process and apoptosis signailg pathway is more significant in groupA....

(NO)



Can we do more detailed analysis?

Differential Expression of RNA-Seq

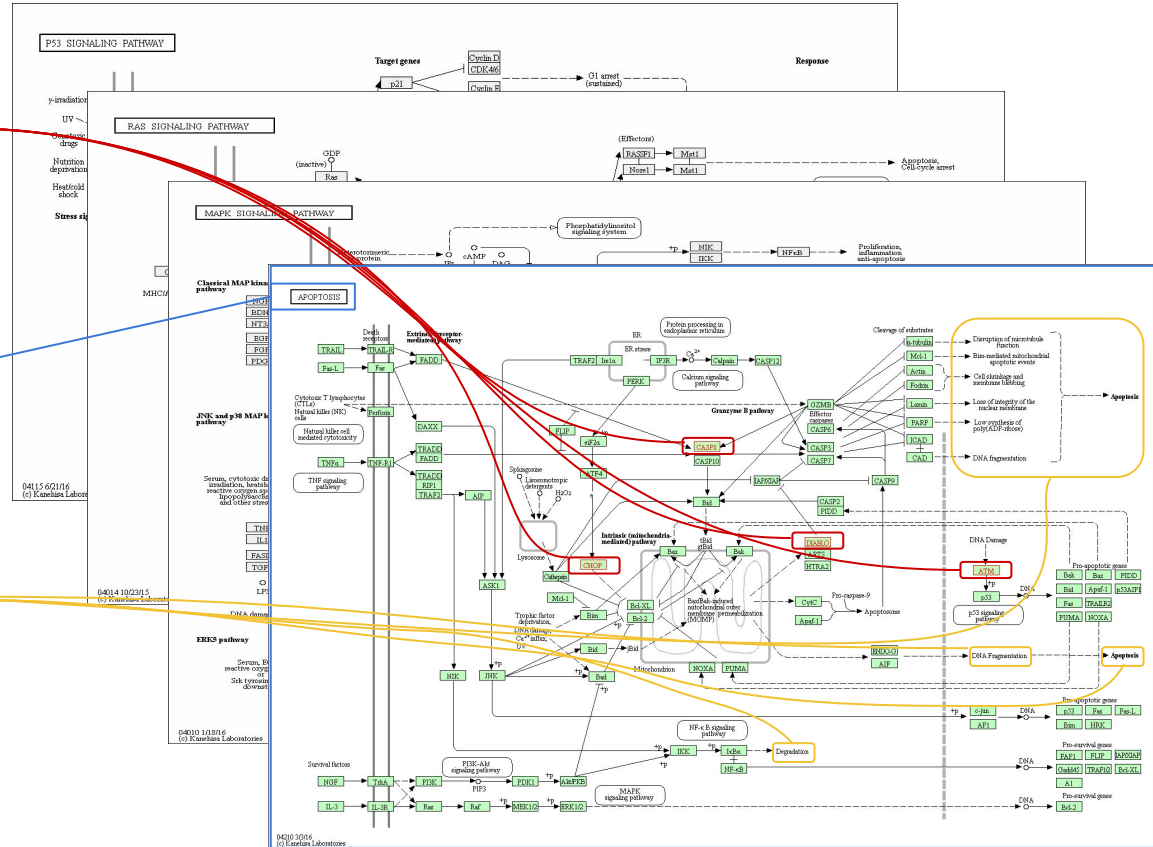
Diff. exp. genes

Functional Profiling: FatiGO and
Gene Set Analysis

Enriched pathway

Signaling Pathways Analysis

Cellular Functions



Cell signaling

Cell signaling (also known as signal transduction) is the transmission of molecular signals from a cell's exterior to its interior.

This process is initiated by cell-surface receptors and terminated by effector protein.

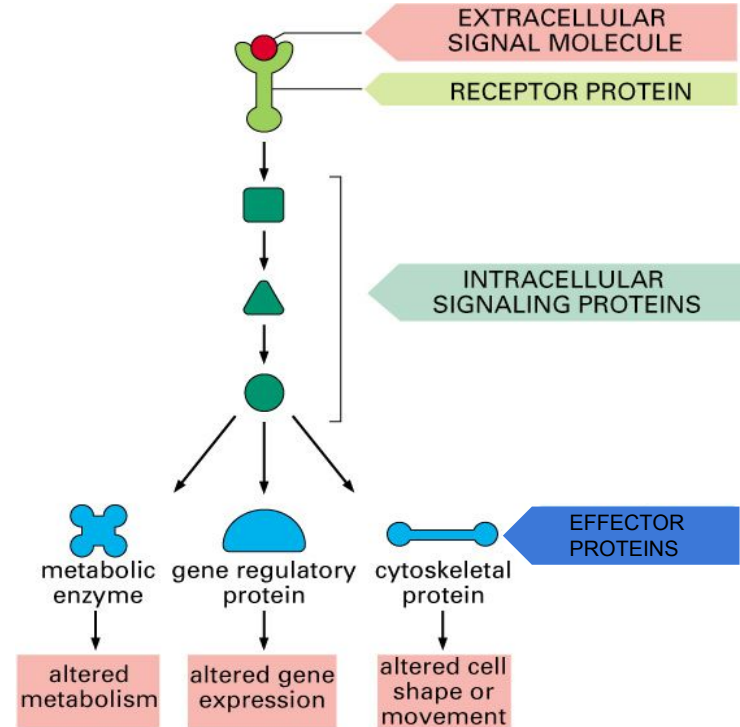


Figure 15–1. Molecular Biology of the Cell, 4th Edition.

Cell signaling

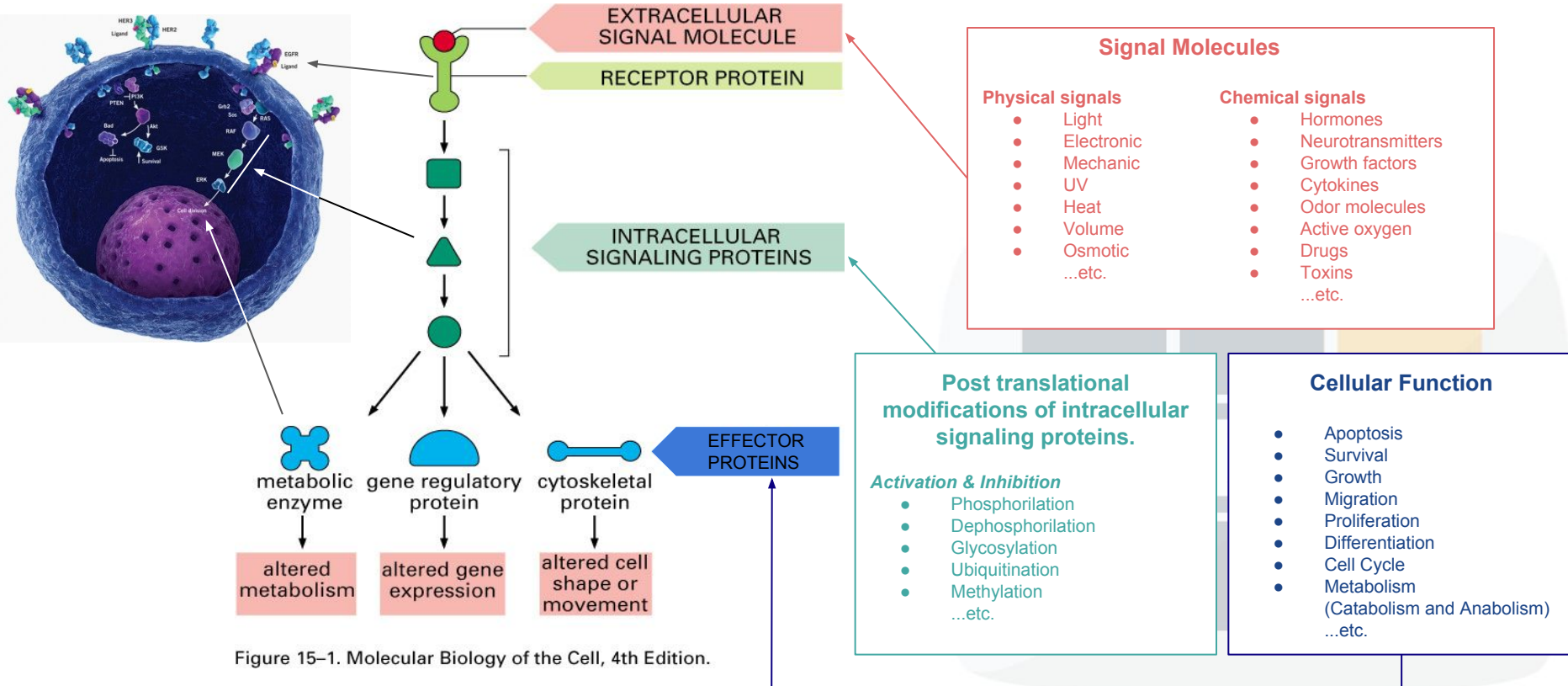


Figure 15–1. Molecular Biology of the Cell, 4th Edition.

Signaling pathways

Signaling pathways (SP) are graphical representations of the interactions of cell signaling components (receptor, intracellular and effector proteins).

Technically:

A component of SP is called *node*.

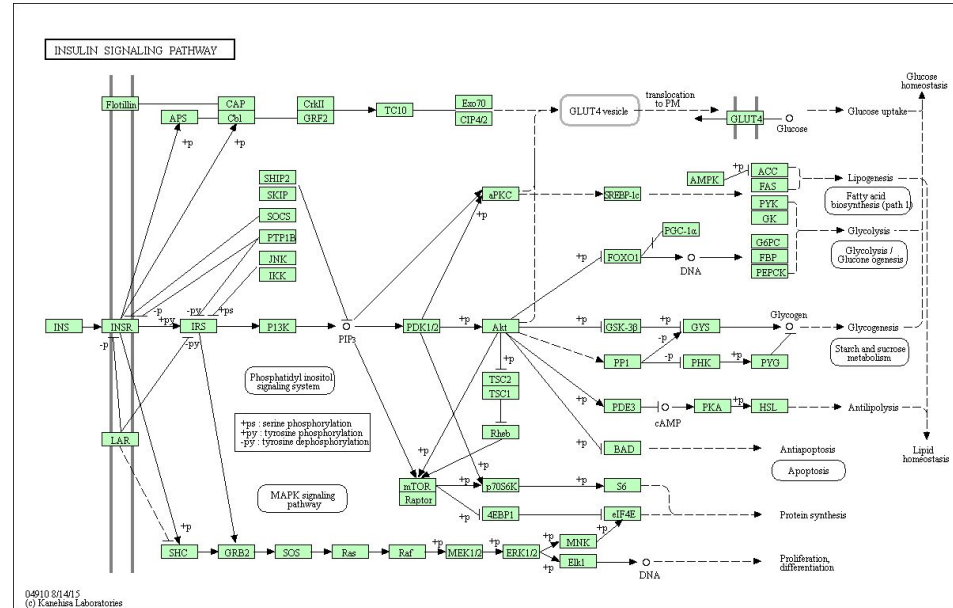
A relation between nodes is called *edge*.

SP formats:

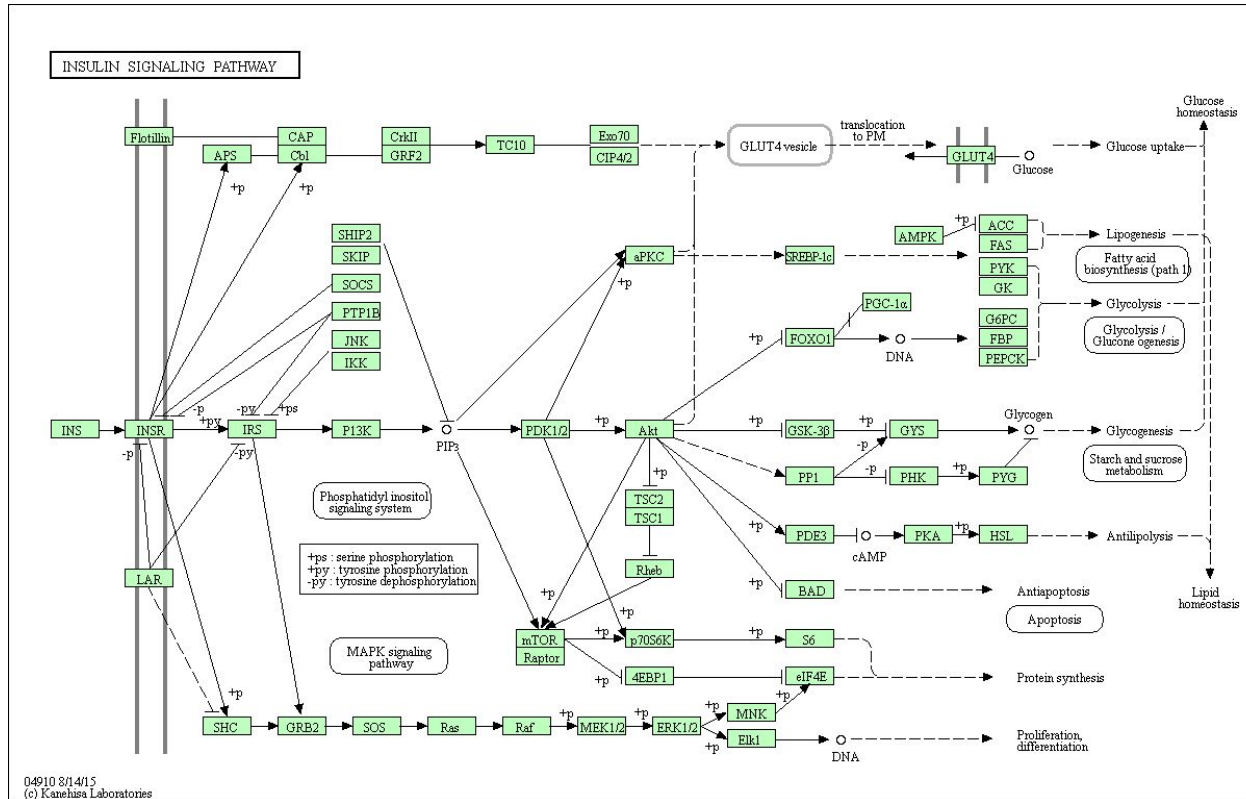
SIF ,KGML, SBML, SBGN, ..., etc.

SP databases:

[KEGG](#), [Reactome](#), [Wikipathways](#), ..., etc.

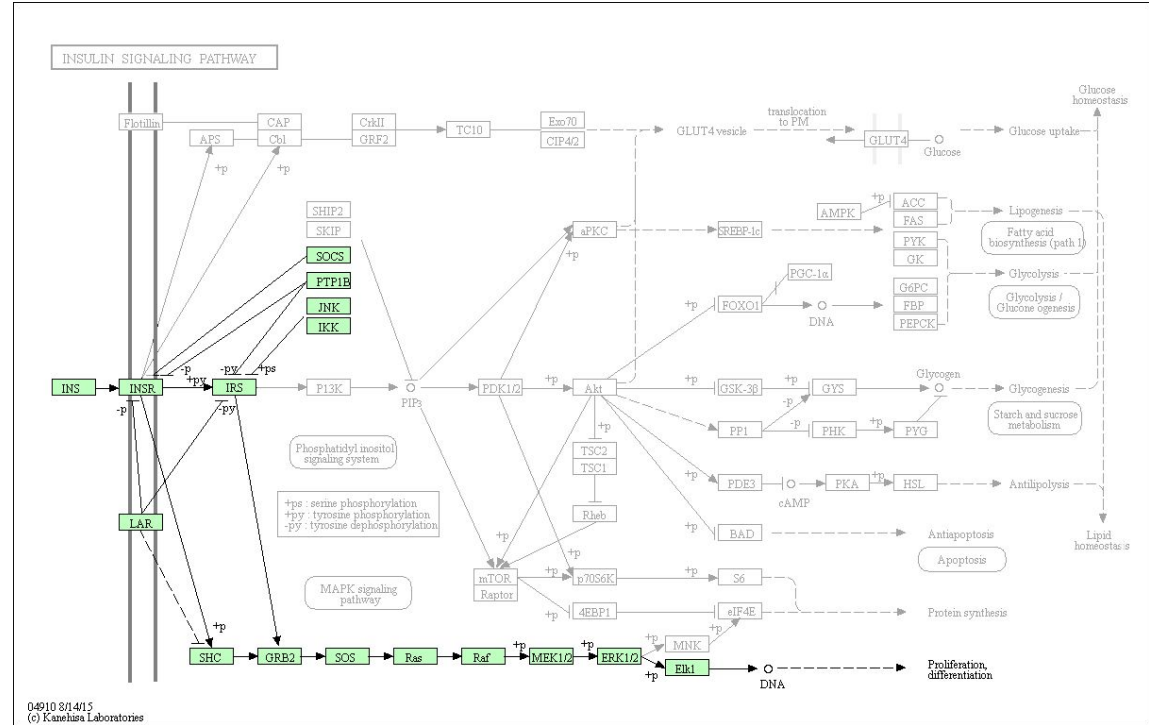
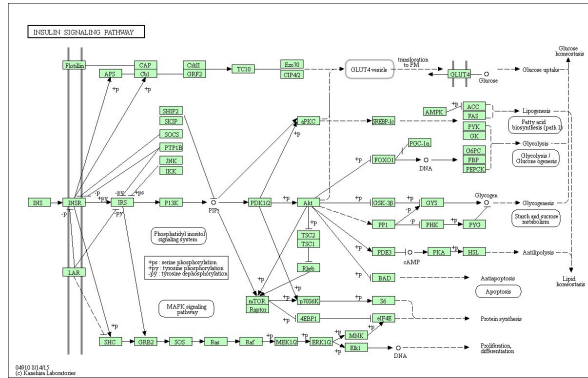


Signaling pathways



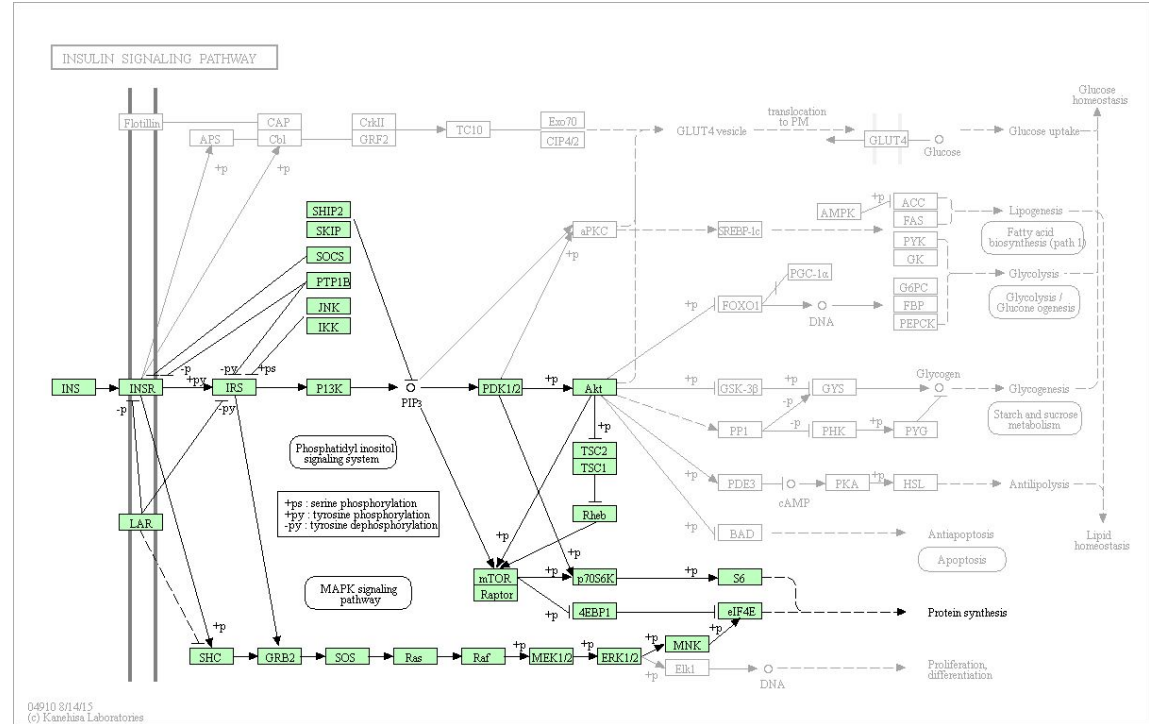
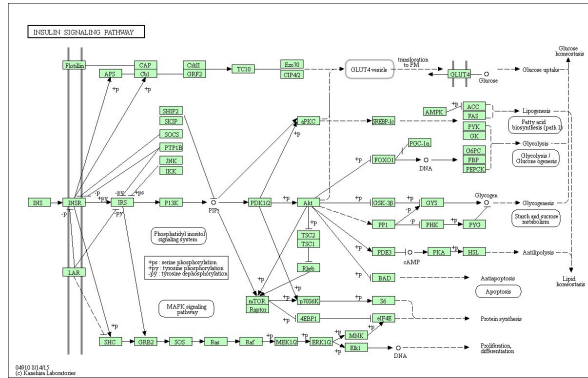
Unpuzzling signaling pathways - Example 1

Propagation of the signal from receptor protein to effector protein on the direction of the edges.



Unpuzzling signaling pathways - Example 2

Propagation of the signal from receptor protein to effector protein on the direction of the edges.



Signaling pathways - Results

Transforming gene expression data into the quantitative cellular functions.

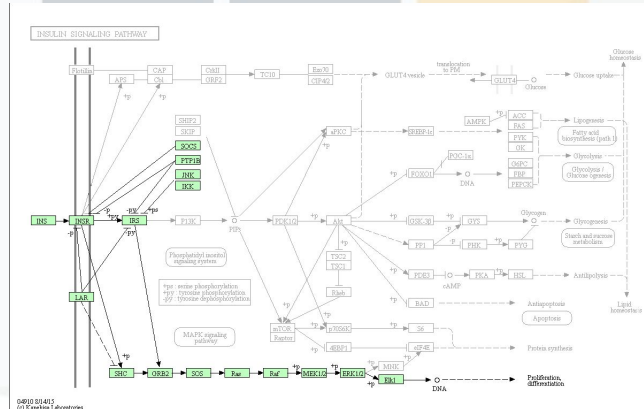
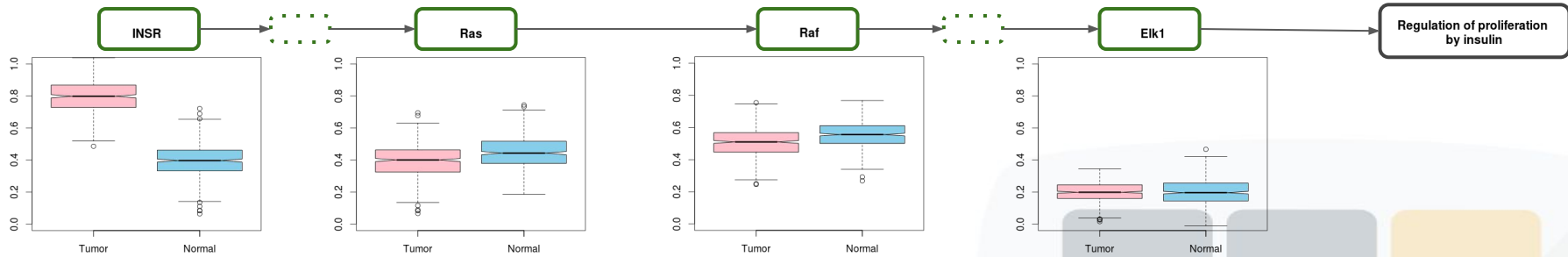
	Sample1	Sample2	Sample3
INS	0.51	0.82	0.44
INSR	0.97	0.83	0.24
...
Ras	0.46	0.44	0.56
Raf	0.54	0.63	0.68
Elk1	0.29	0.17	0.15



		Sample1	Sample2	Sample3
Insulin Signaling Pathway	Apoptosis	0.82	0.93	0.87
	Proliferation	0.58	0.57	0.54
	Glycogenesis	0.83	0.95	0.48

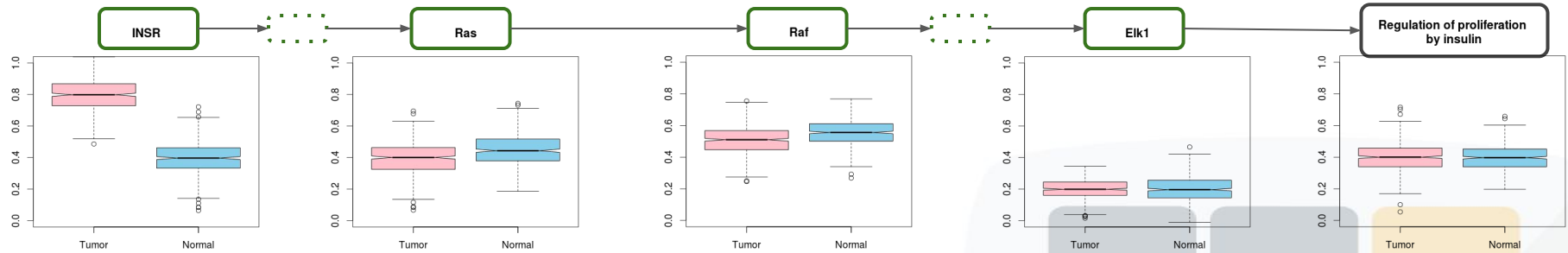
Signaling pathways - Results - Interpretation

Transforming gene expression data into the quantitative cellular functions.



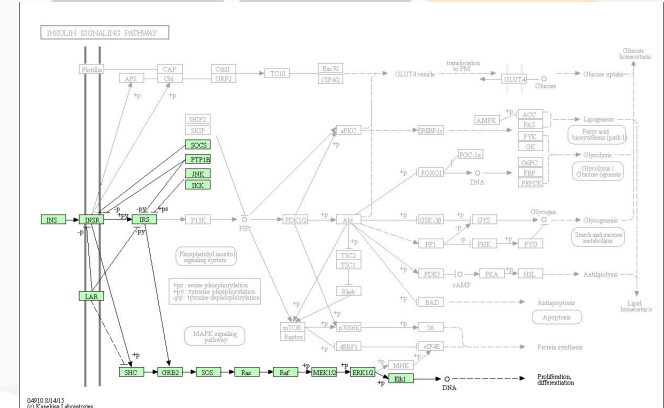
Signaling pathways - Results - Interpretation

Transforming gene expression data into the quantitative cellular functions.



Will INSR gene be your target to control proliferation?

The effect of the INSR is compensated by other genes which are in the same cascade.



hiPathia

Transforming gene expression data into quantitative cellular functions.

	Sample1	Sample2	Sample3
INS	0.5	0.8	0.4
INSR	0.9	0.2	0.6
...
Ras	0.2	0.5	0.8
Raf	0.9	0.8	0.5
Elk1	0.5	0.1	0.6

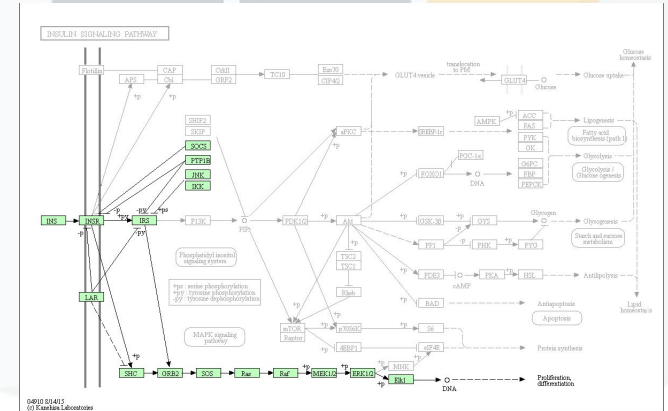
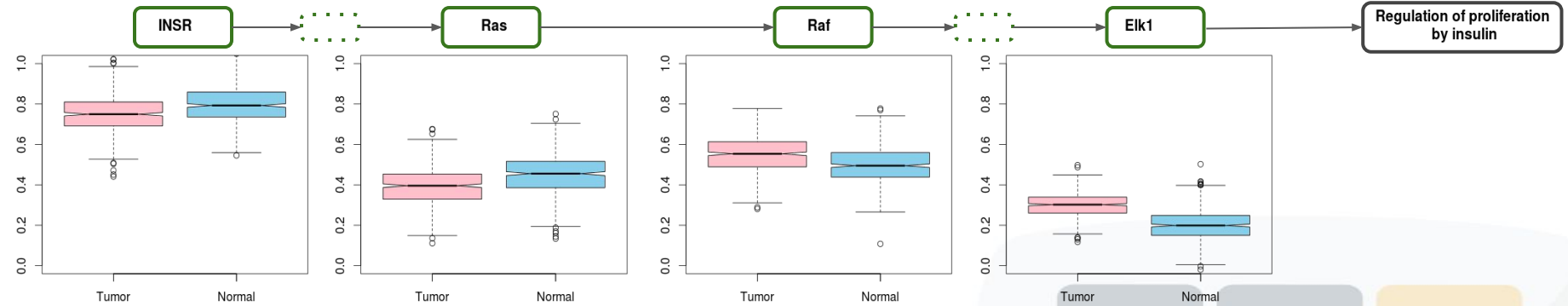


		Sample1	Sample2	Sample3
Insulin Signaling Pathway	Apoptosis	0.8	0.9	0.1
	Proliferation	0.5	0.6	0.8
	Glycogenesis	0.5	0.9	0.4

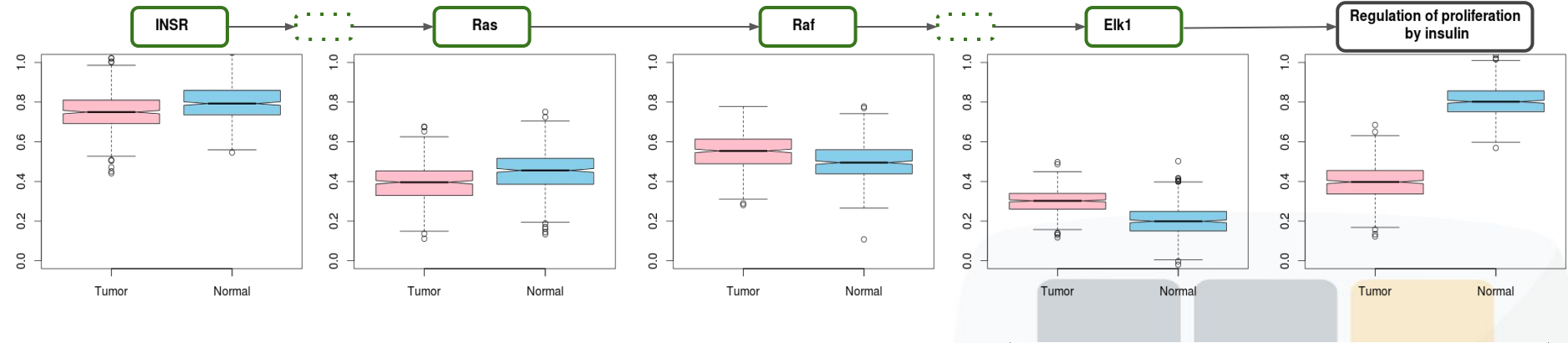
<http://hipathia.babelomics.org/>



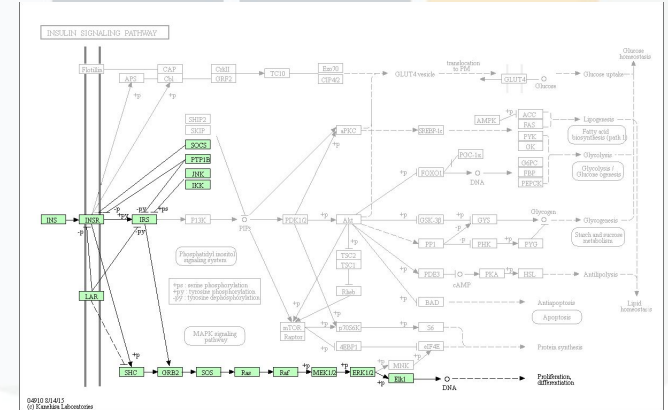
Signaling pathways - Insilico approaches



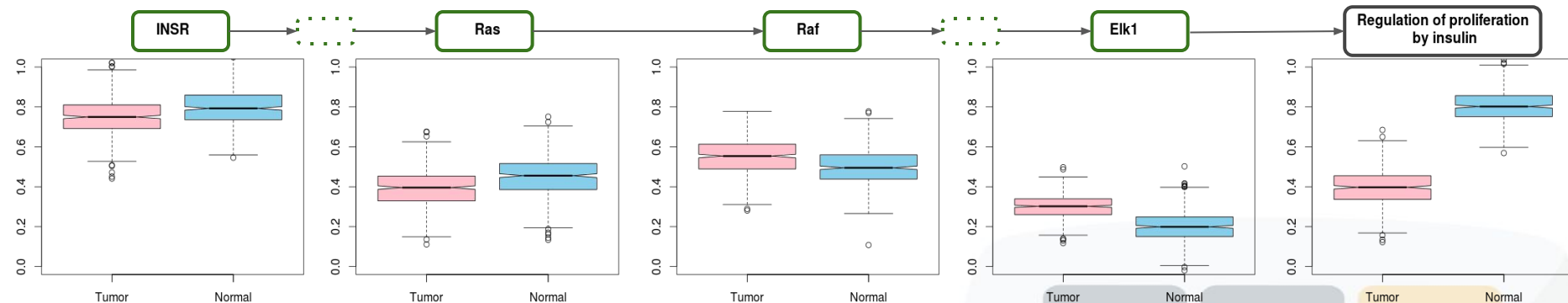
Signaling pathways - Insilico approaches



Is it worth to focus on this part of insulin signaling pathway to control proliferation?



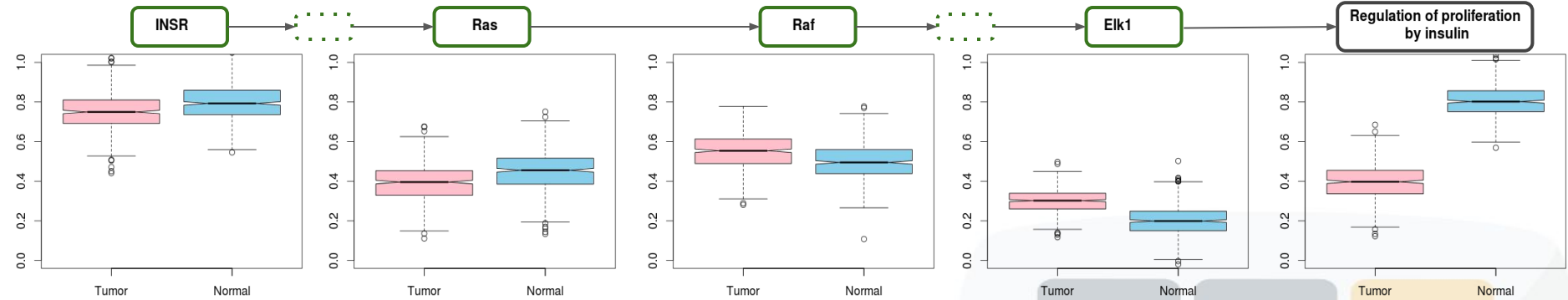
Signaling pathways - Insilico approaches - How



- Simulating drug effects
Single drug
Drug cocktails
- Gene interventions
Knockdowns
Over-expressions

DRUGBANK
Drug & Drug Target Database

Signaling pathways - Insilico approaches - How



PathAct

<http://pathact.babelomics.org/>





THANKS

