

# Pathways analysis

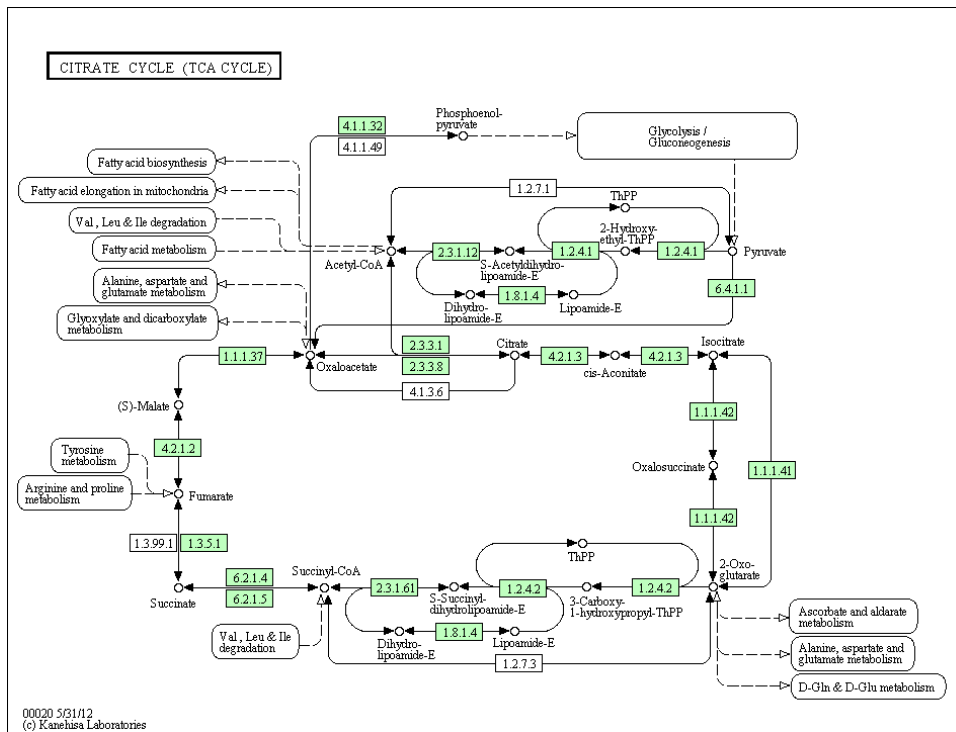
Patricia Sebastián León  
psebastian@cipf.es



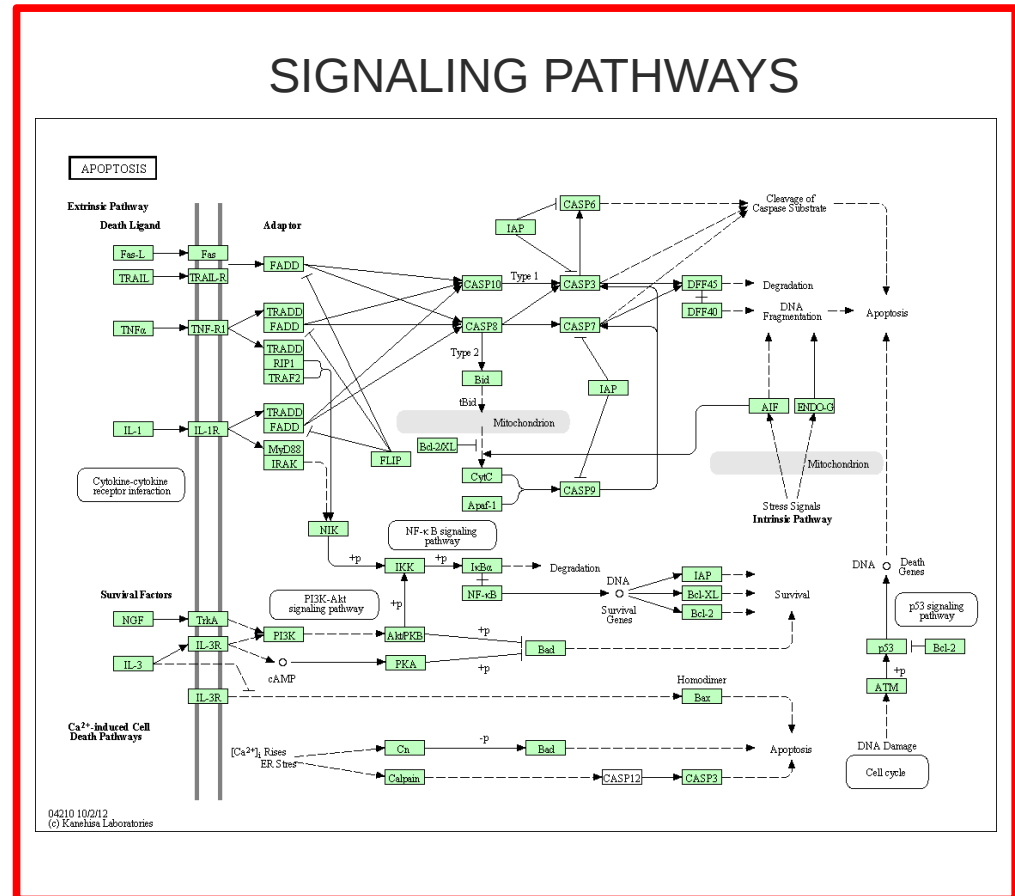
# Introduction

PATHWAY = Series of actions among molecules in a cell that leads to a certain product or a change in a cell

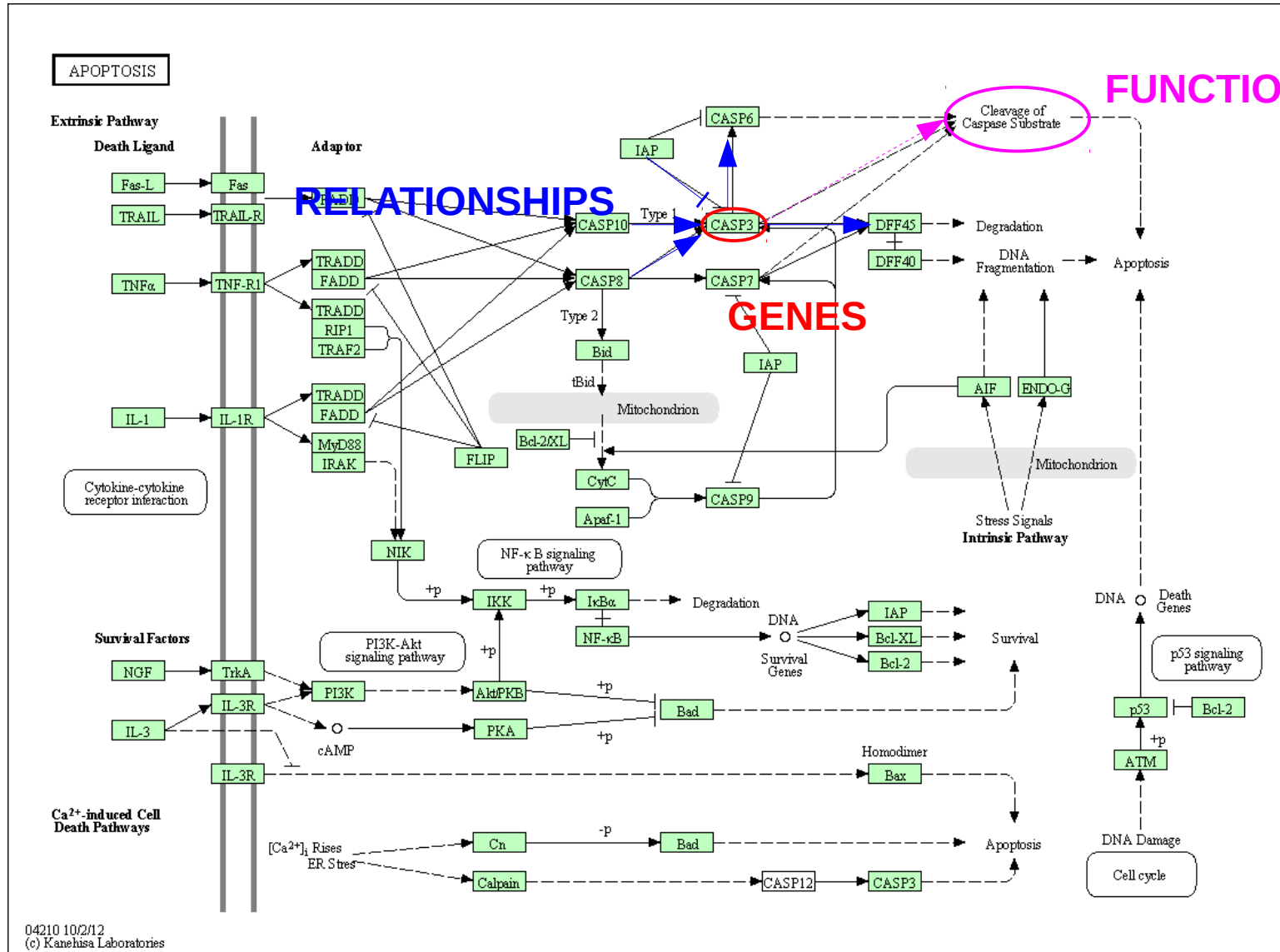
## METABOLIC PATHWAYS



## SIGNALING PATHWAYS

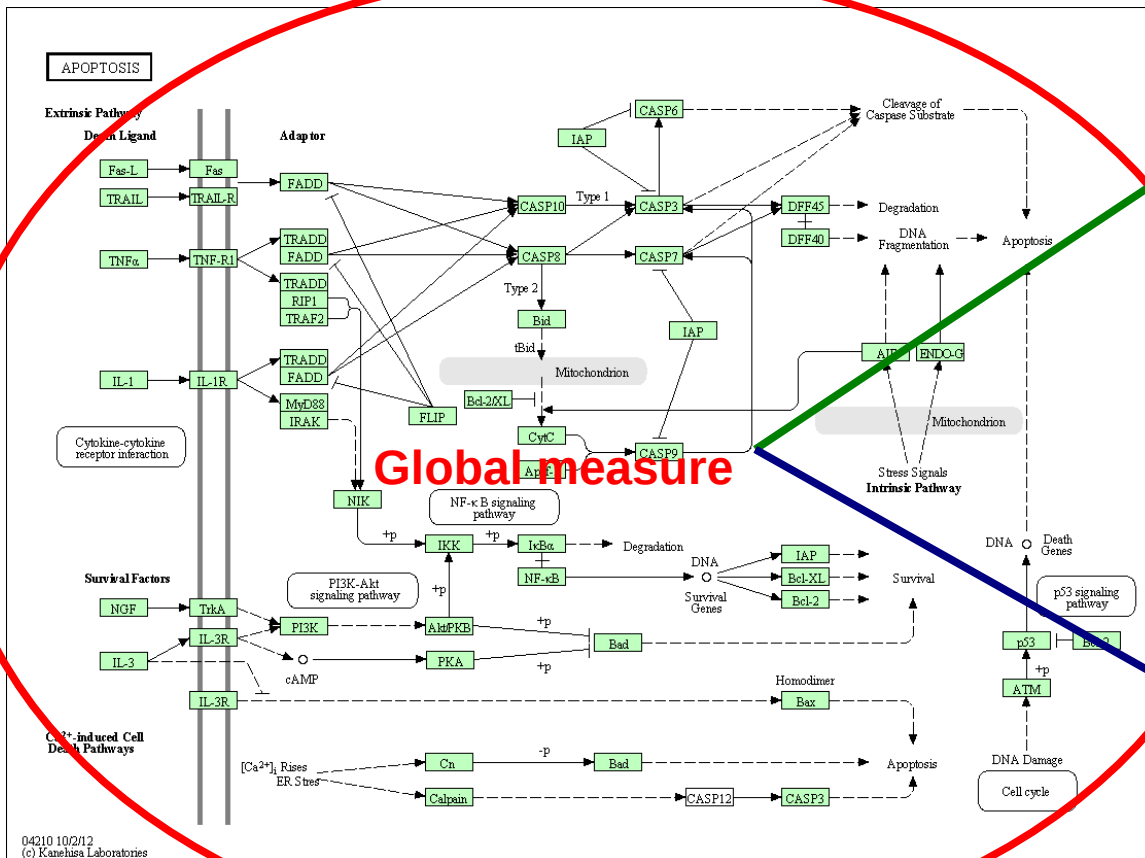


# KEGG



04210 10/2/12  
 (c) Kanehisa Laboratories

# Current methods



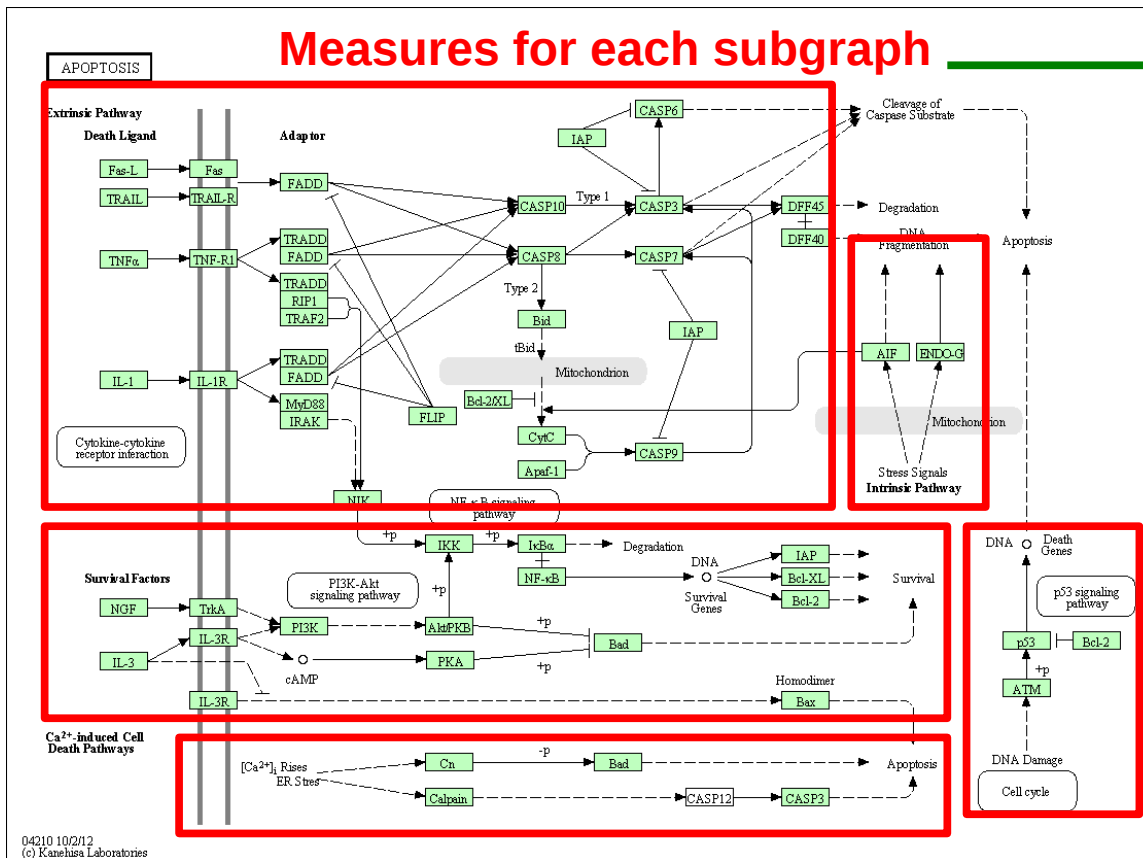
**Set of genes:**

- Gene Set Enrichment Analysis (GSEA methods)
- ...

**Network with structure:**

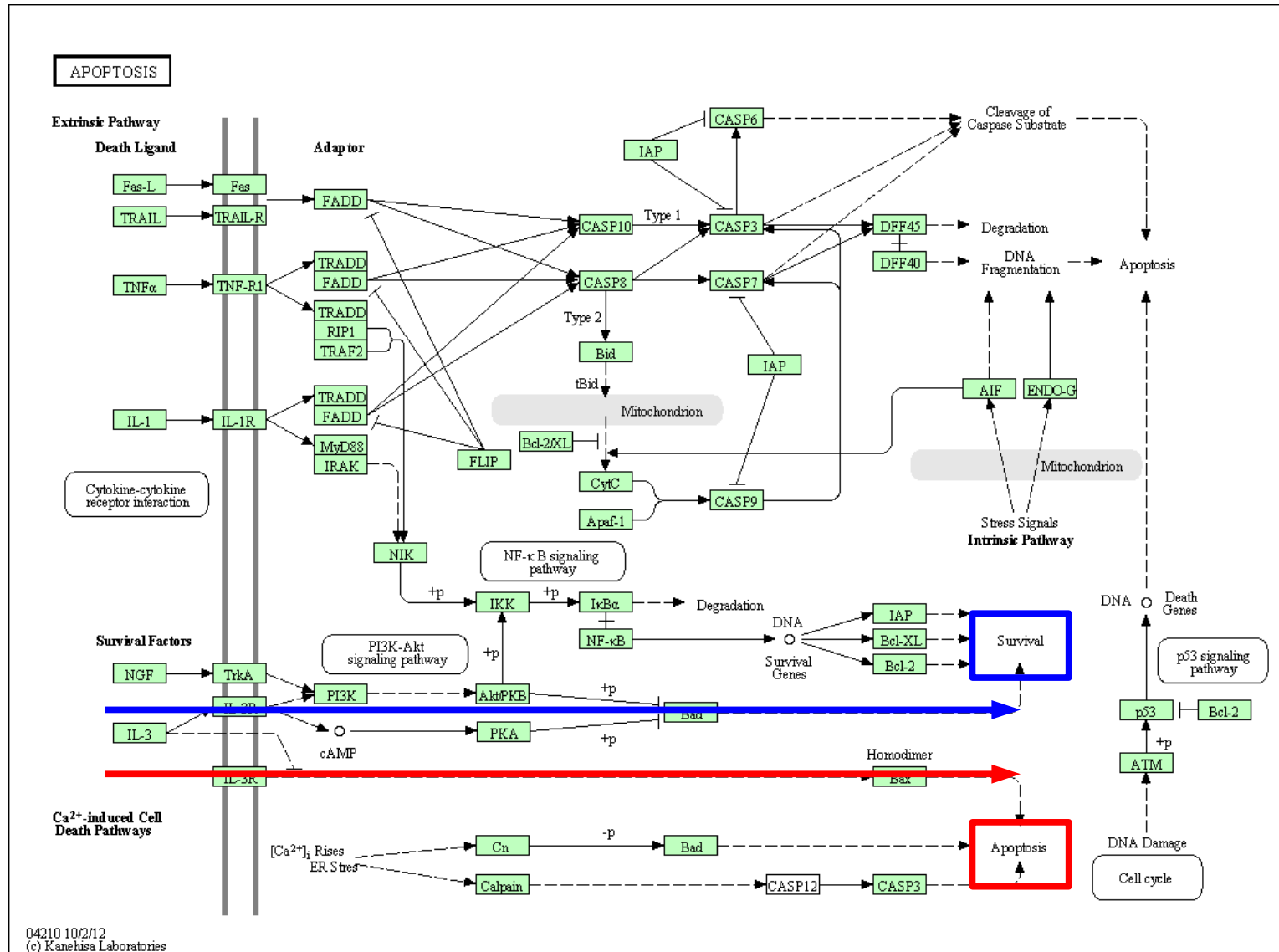
- Signaling Pathway Impact Analysis (SPIA)
- ...

# Current methods

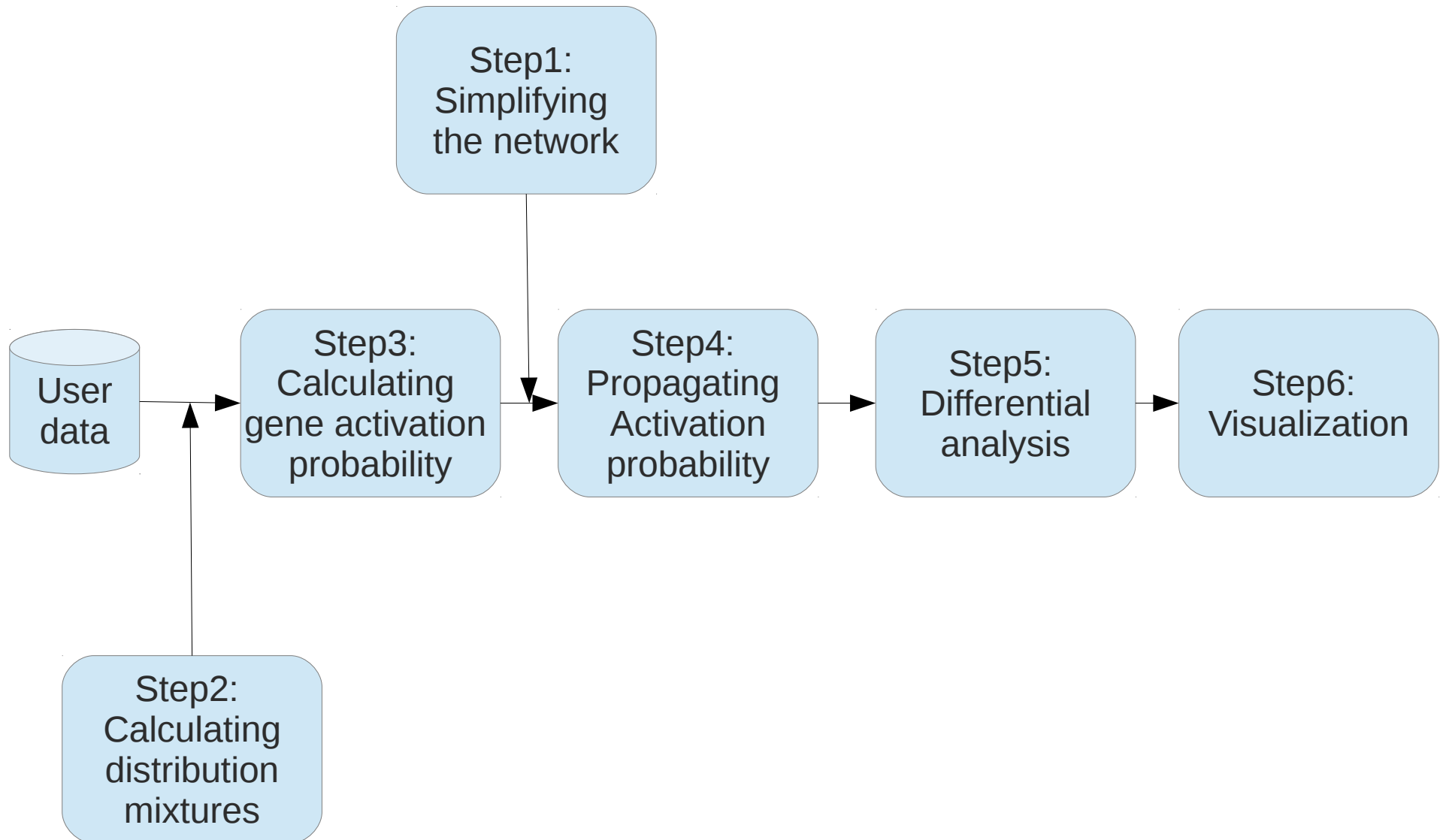


- ClipperDevel
- DEGraph
- ...

# But...

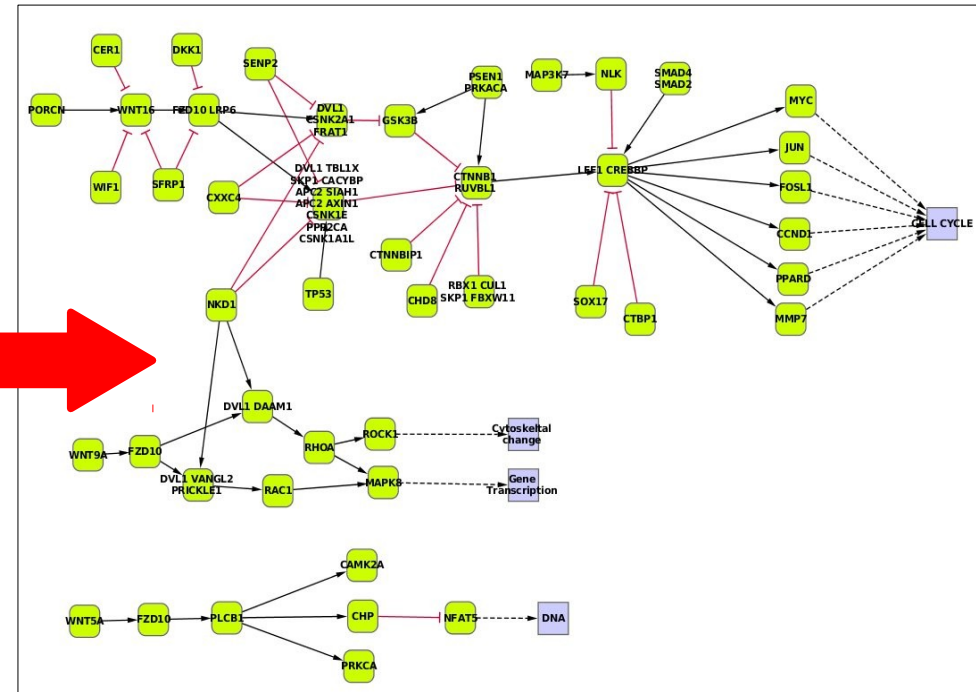
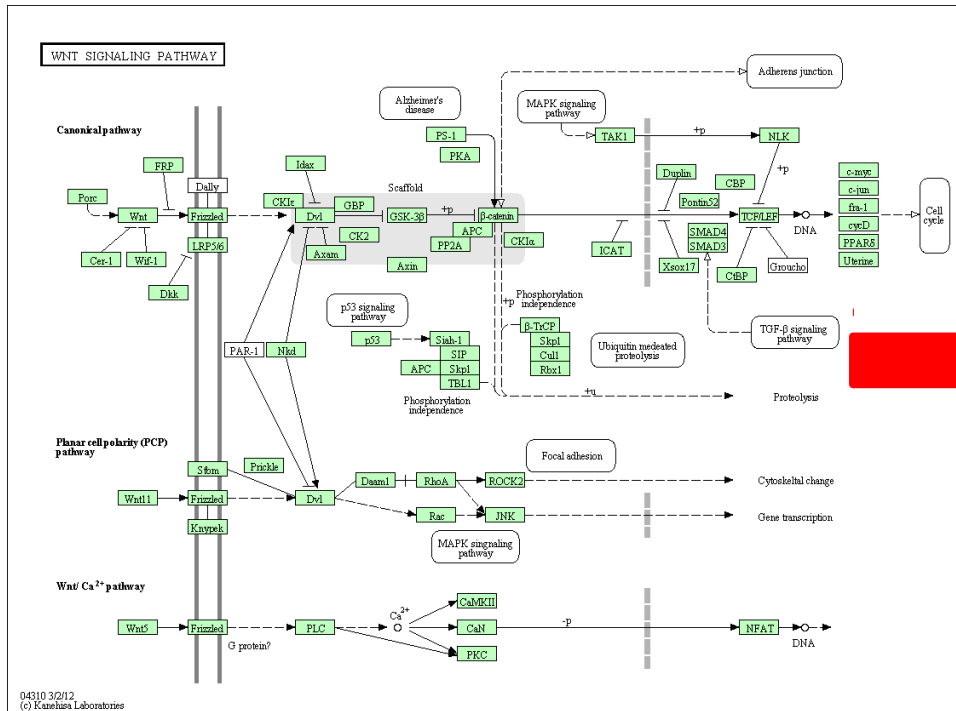


# Pathway analysis - Pipeline



# Pathways analysis – Step 1

## Simplifying pathway network

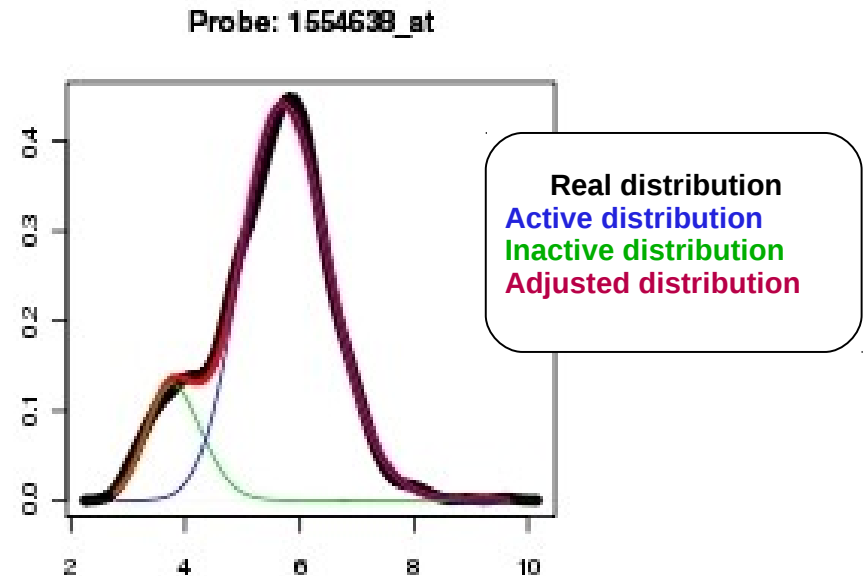
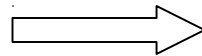
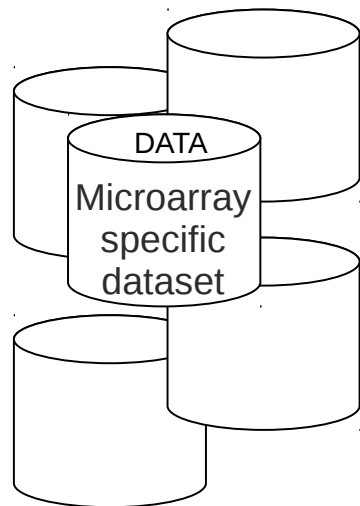


- **ACTIVATION:** Activation, Phosphorilation, Indirect, Expression, Compound, Dephosphorilation, Methylation
- **INHIBITION:** Inhibition, Ubiquination
- **GROUP:** Group, Binding/Association



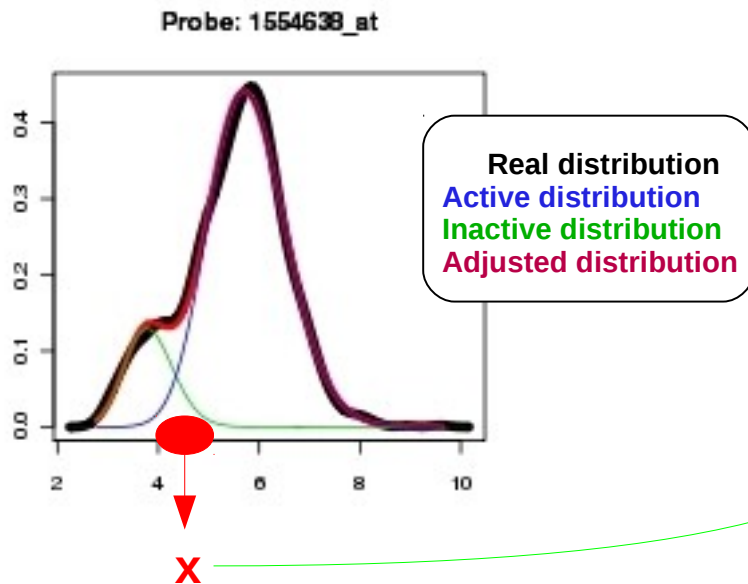
# Pathways analysis – Step 2

Calculating active/inactive distributions for each gene



# Pathways analysis – Step 3

From expression data to gene activation probability data



Considering  $x$  the expression value:

$$P(\text{Activated}|x) = \frac{\Pi_1 f_1(x)}{\Pi_0 f_0(x) + \Pi_1 f_1(x)}$$

Where:

- $f_1$  = Active distribution
- $f_2$  = Inactive distribution
- $\Pi$  = Proportions in the population for each distribution

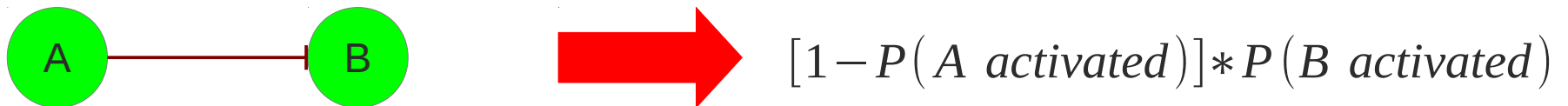
# Pathways analysis – Step 4

From gene to subpathway activation probability

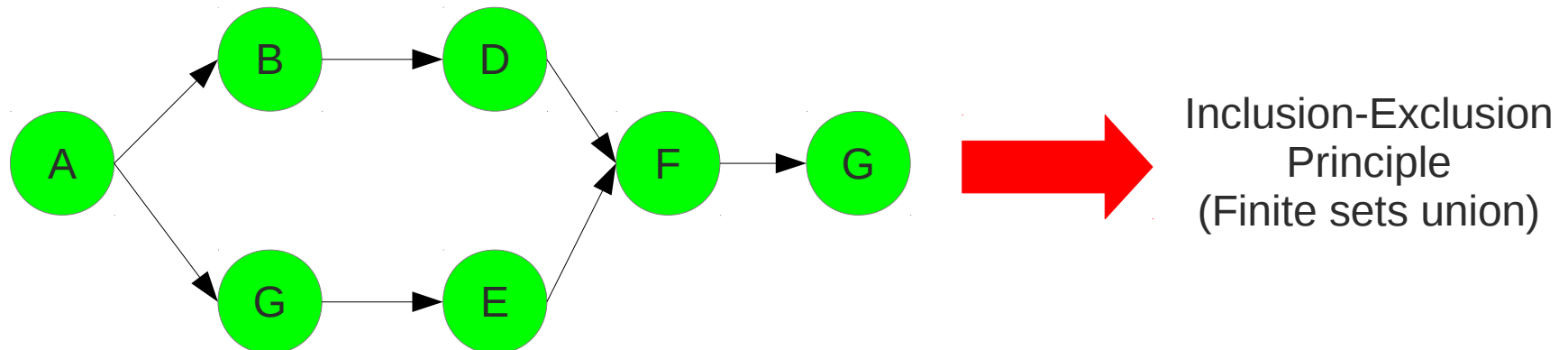
Activation:



Inhibition:



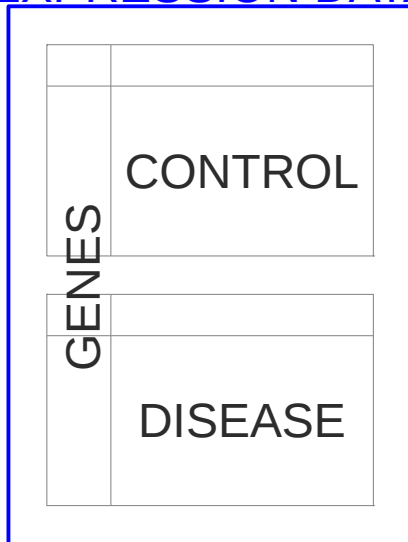
Multiple paths:



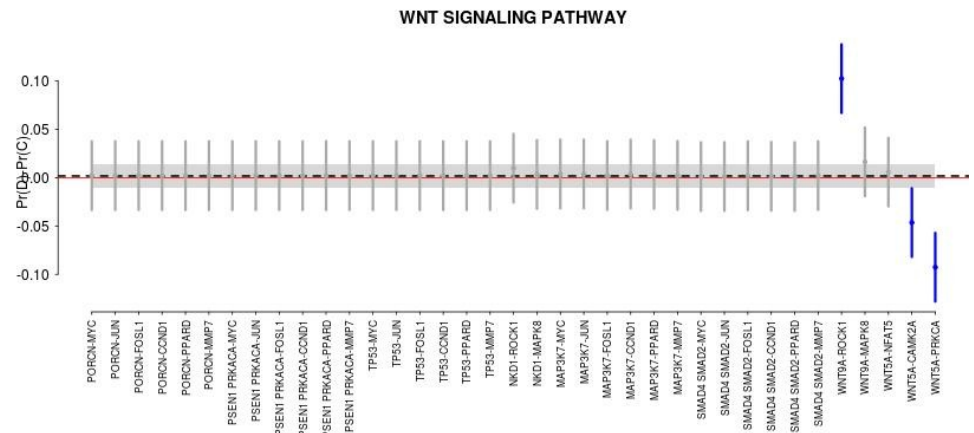
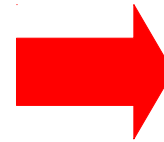
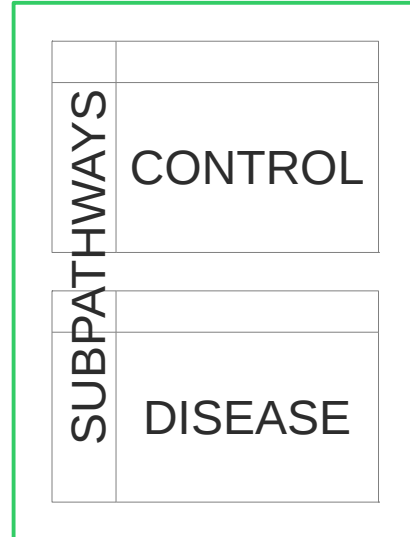
# Pathways analysis – Step 5

## Differential subpathway activation analysis

### EXPRESSION DATA

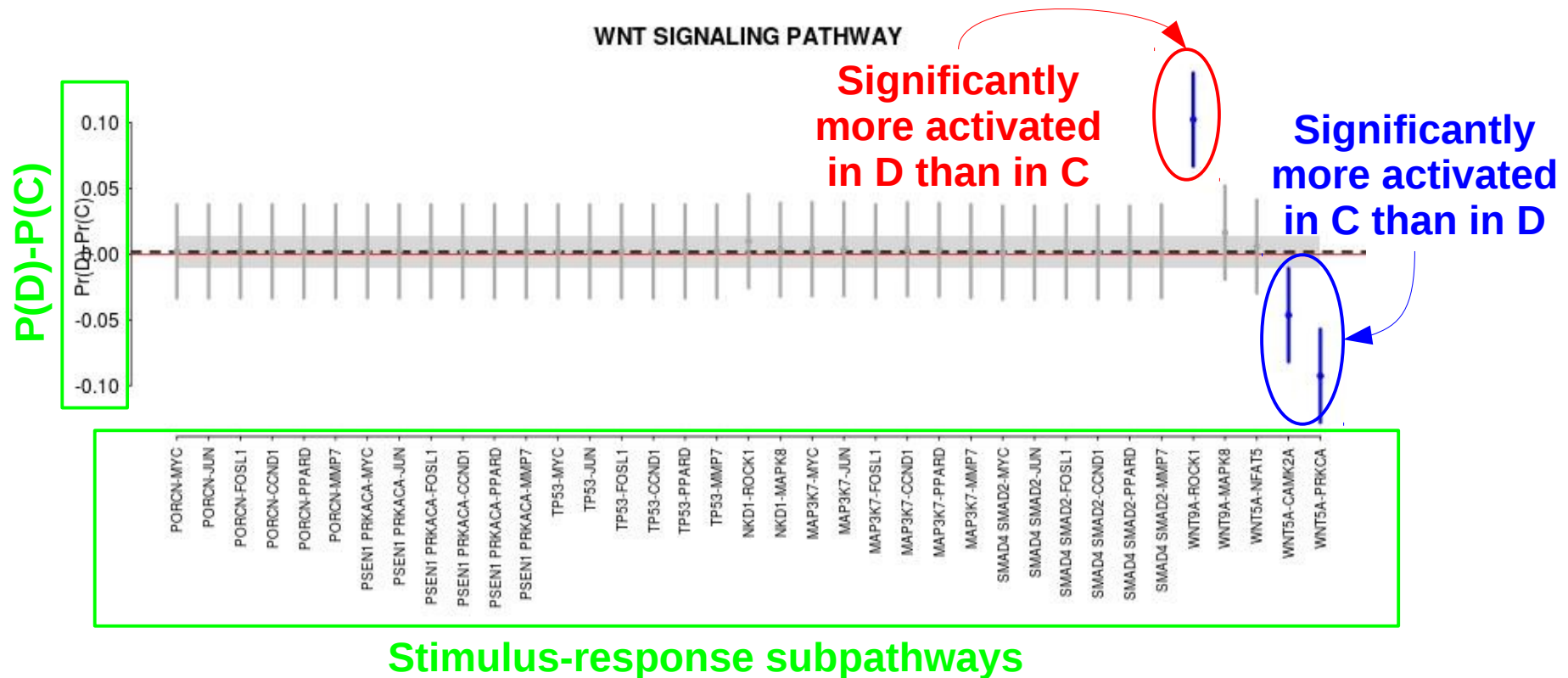


### ACTIVATION PROBS.



# Pathways analysis – Step 5

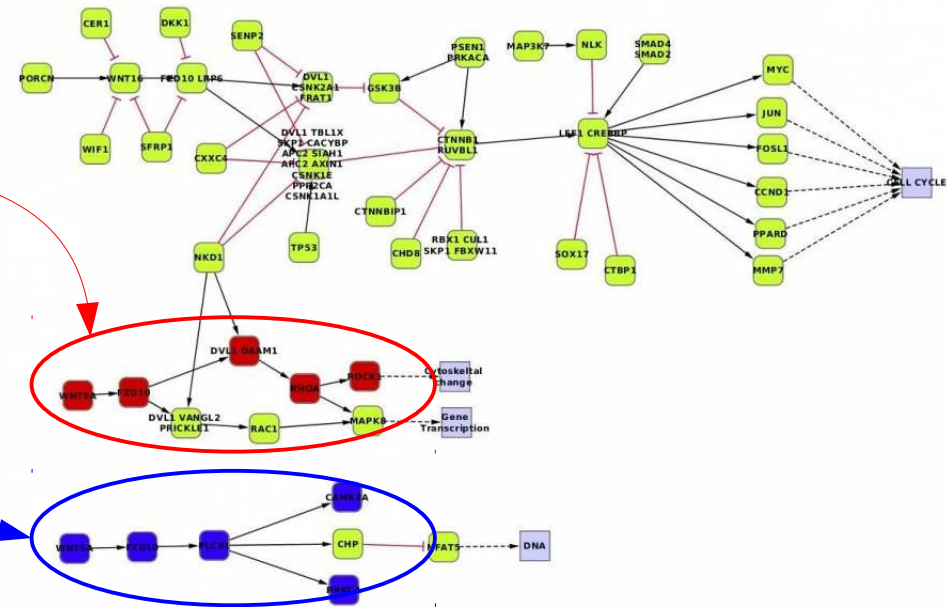
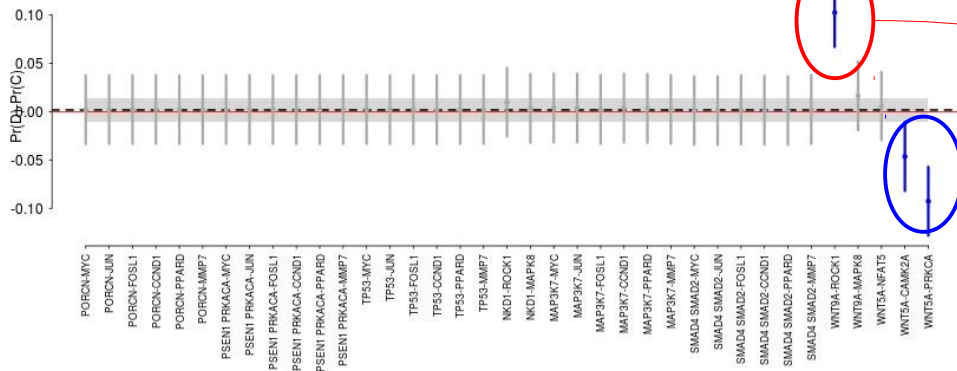
## Differential subpathway activation analysis



# Pathways analysis – Step 6

## Visualization

WNT SIGNALING PATHWAY



# Practical example

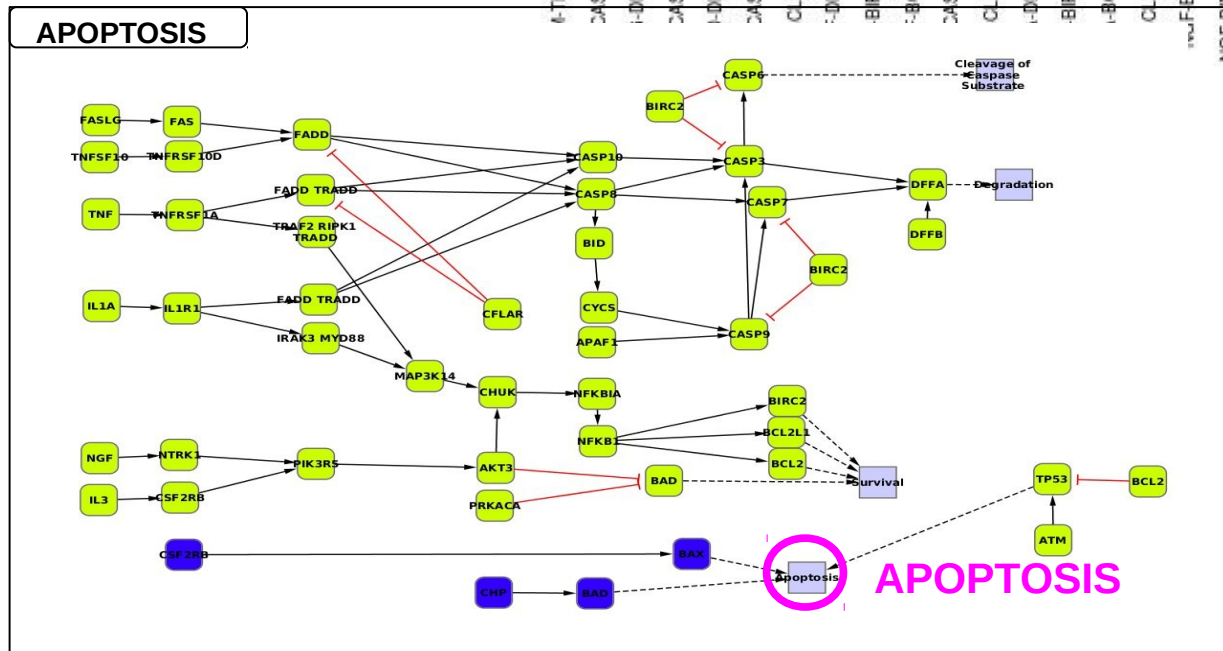
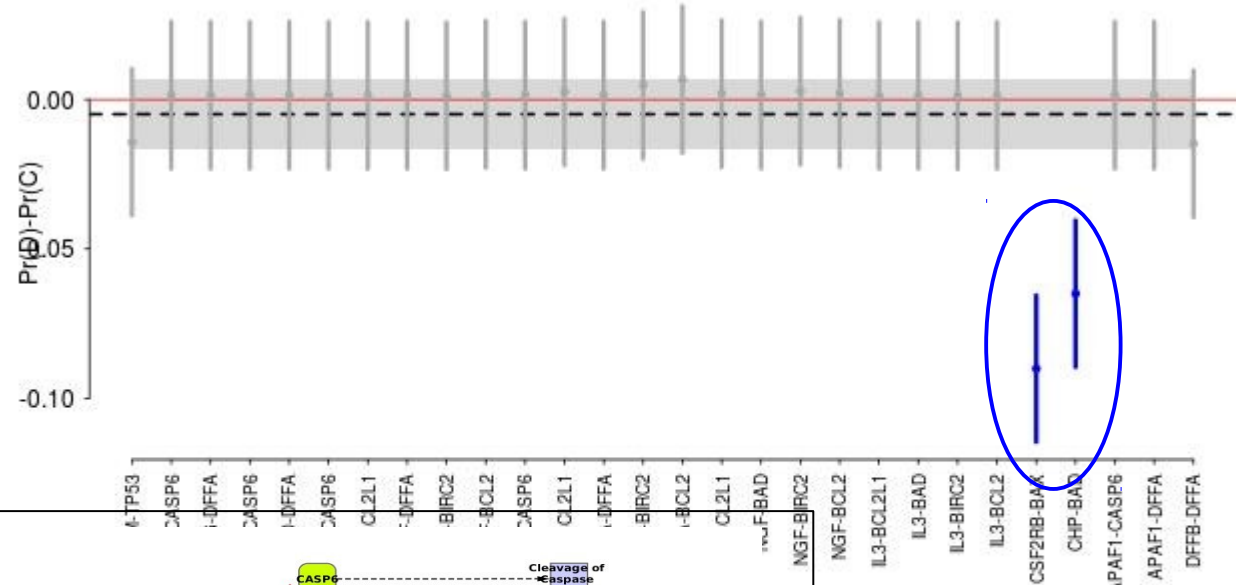
## Colorectal cancer.

GEO experiment:

(Affymetrix™ array HG-U133 Plus2.0)

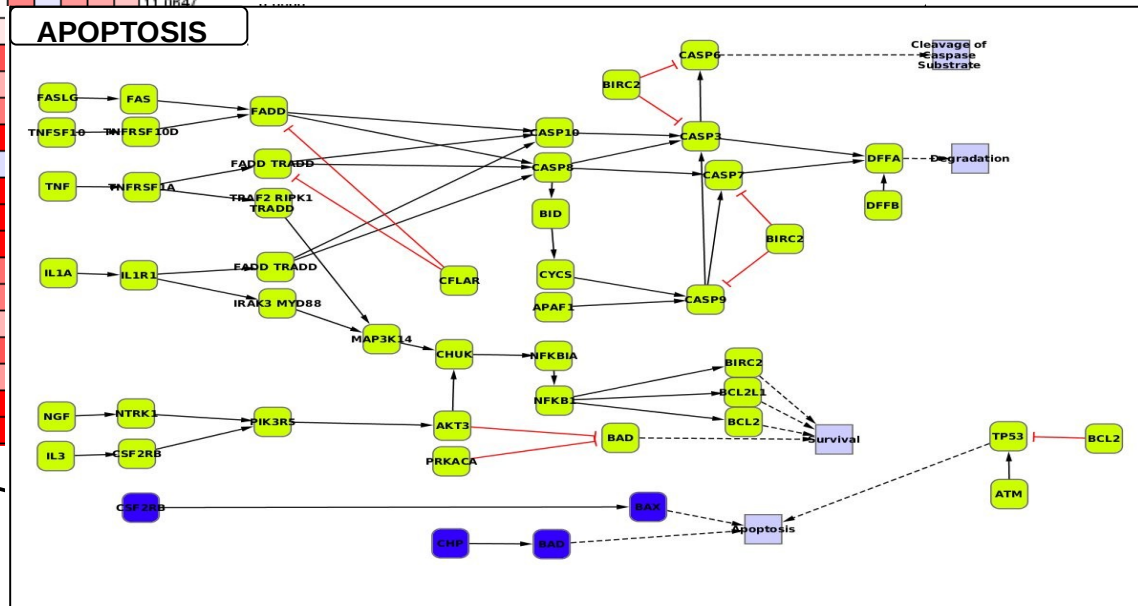
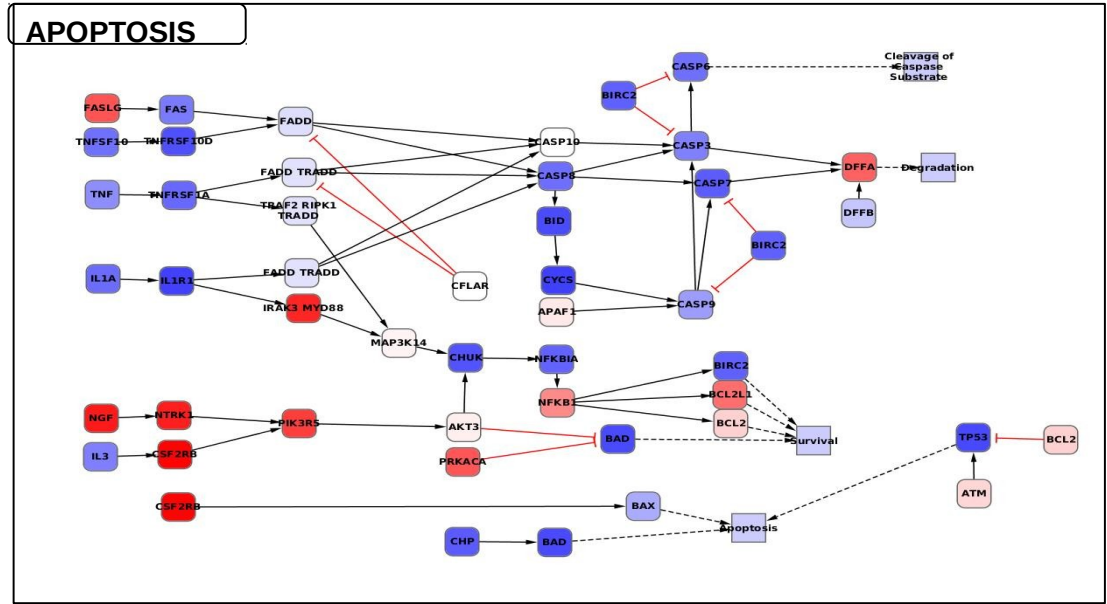
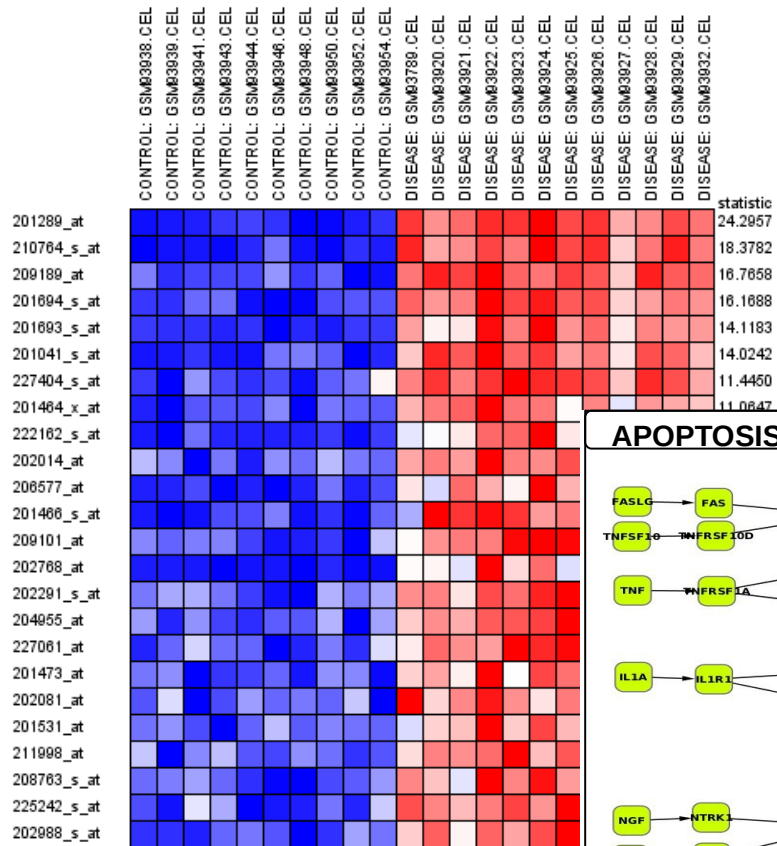
- 12 CRC cases
- 10 healthy controls

## APOPTOSIS



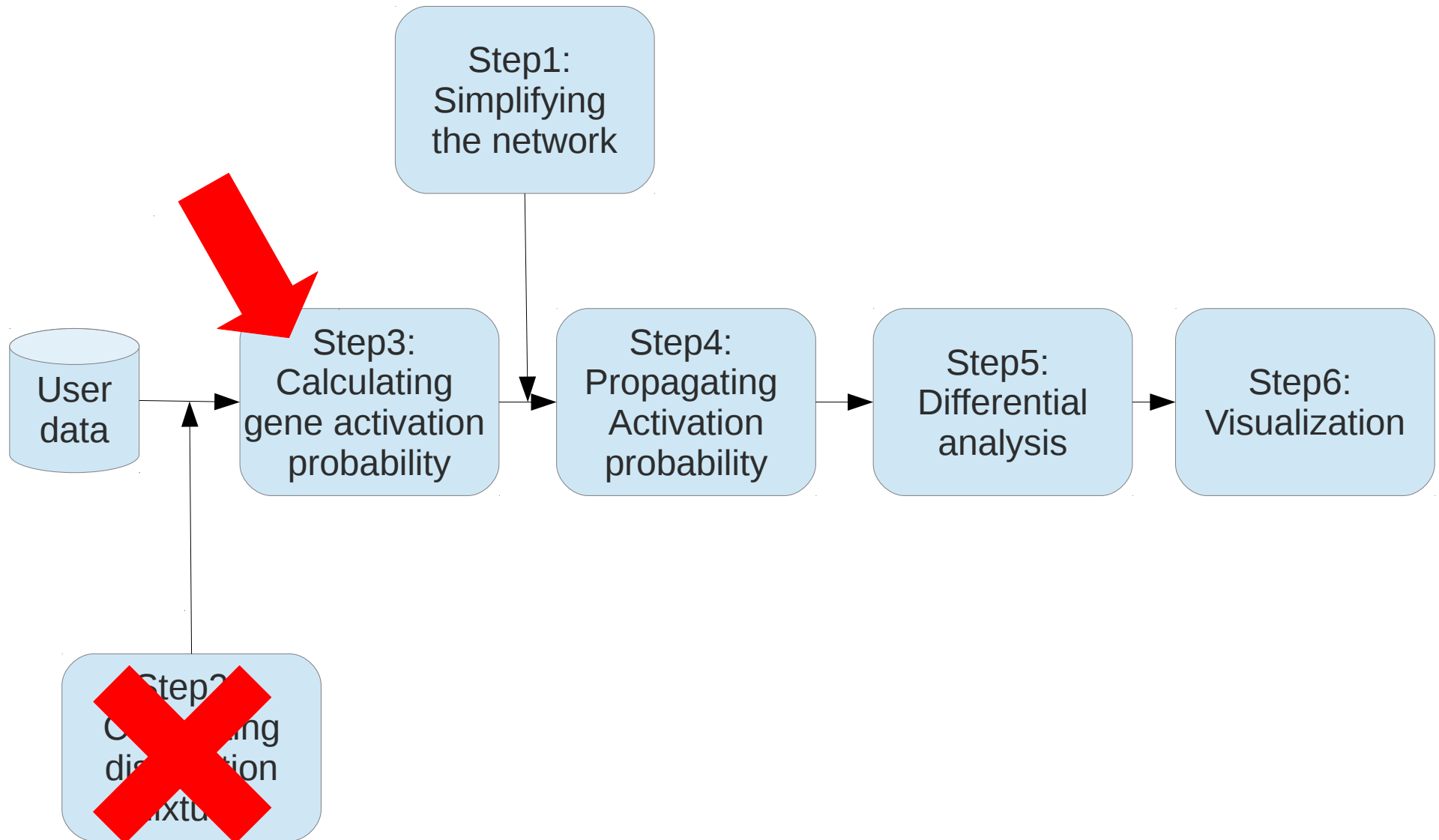
# Practical example

## Class comparison

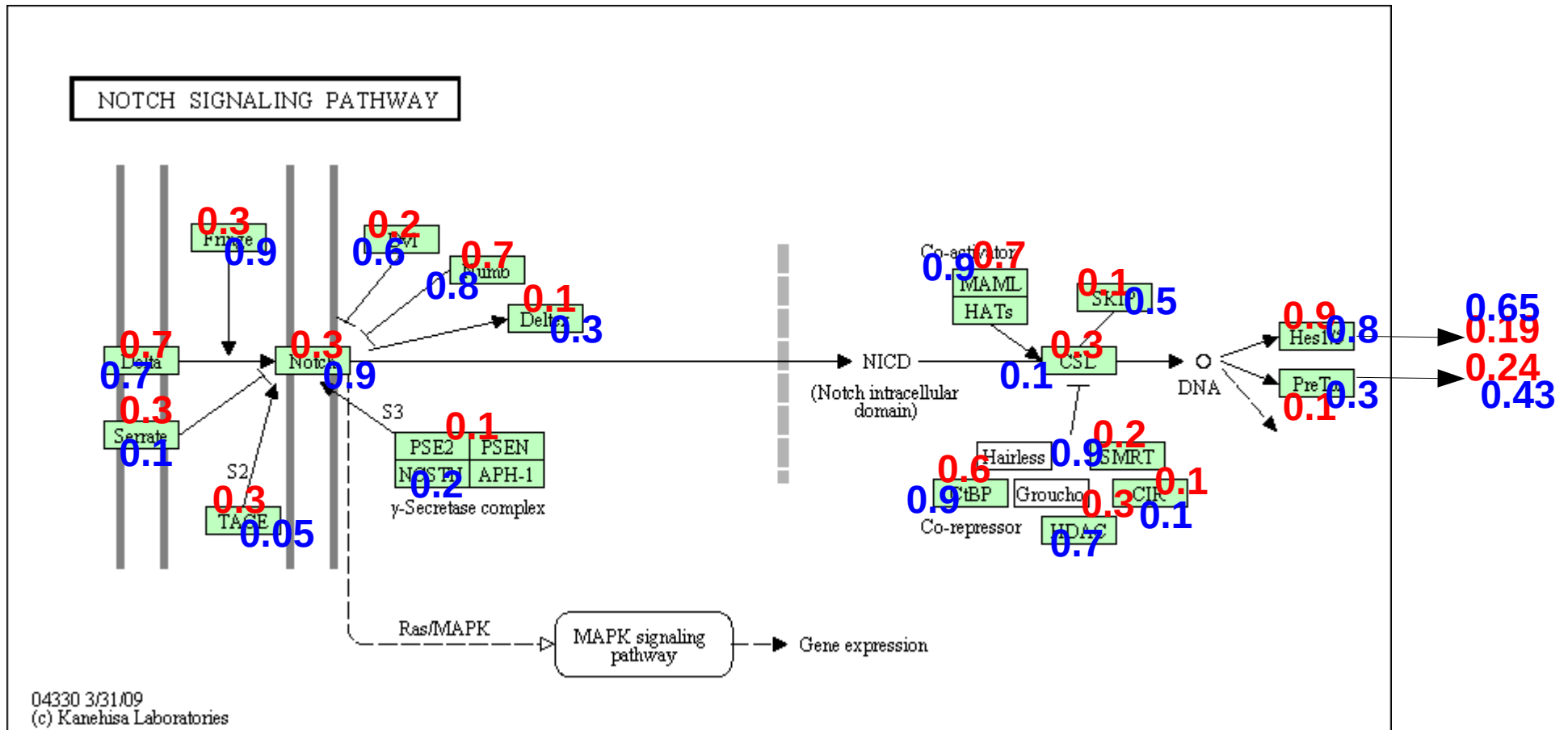




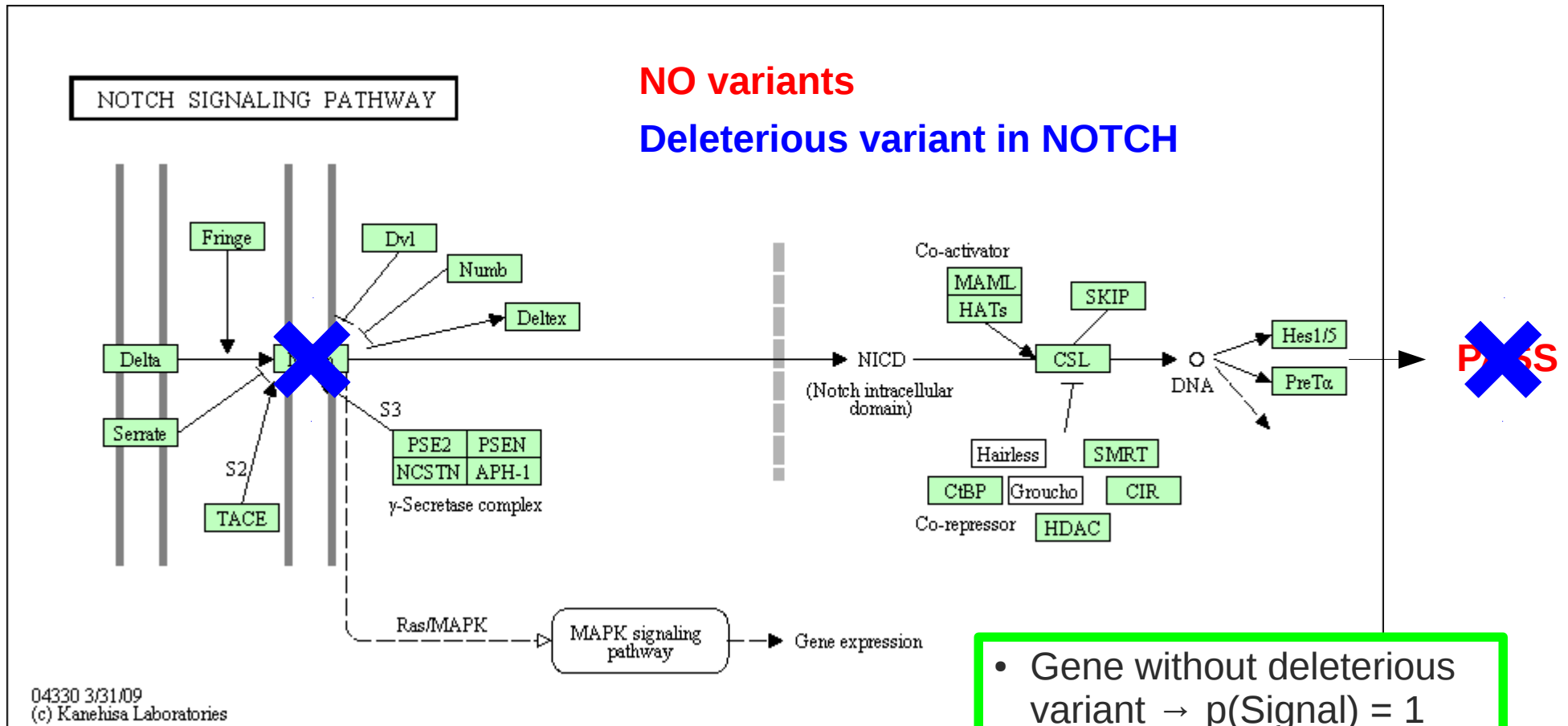
# Pathway analysis - Pipeline



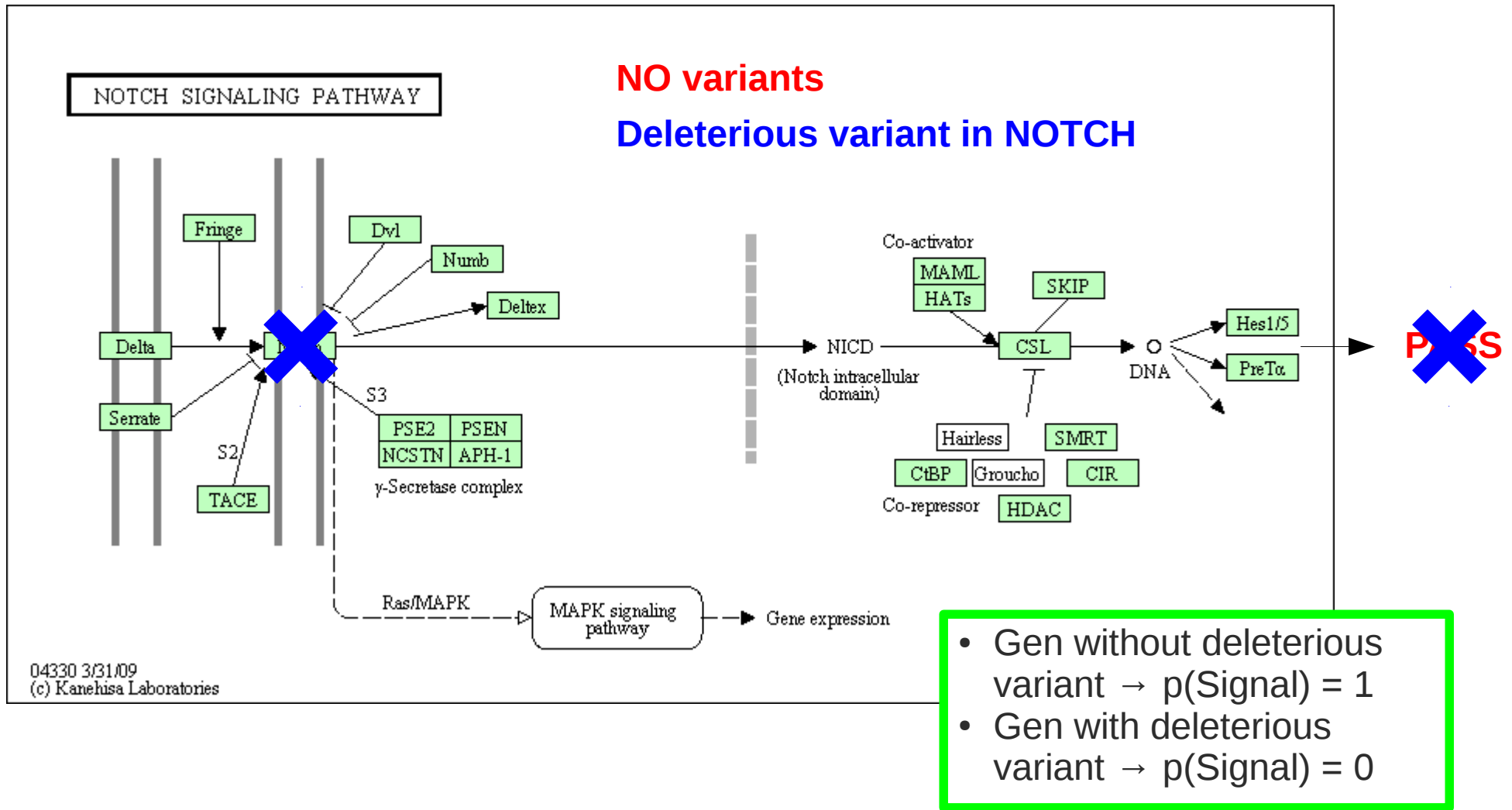
# Expression data



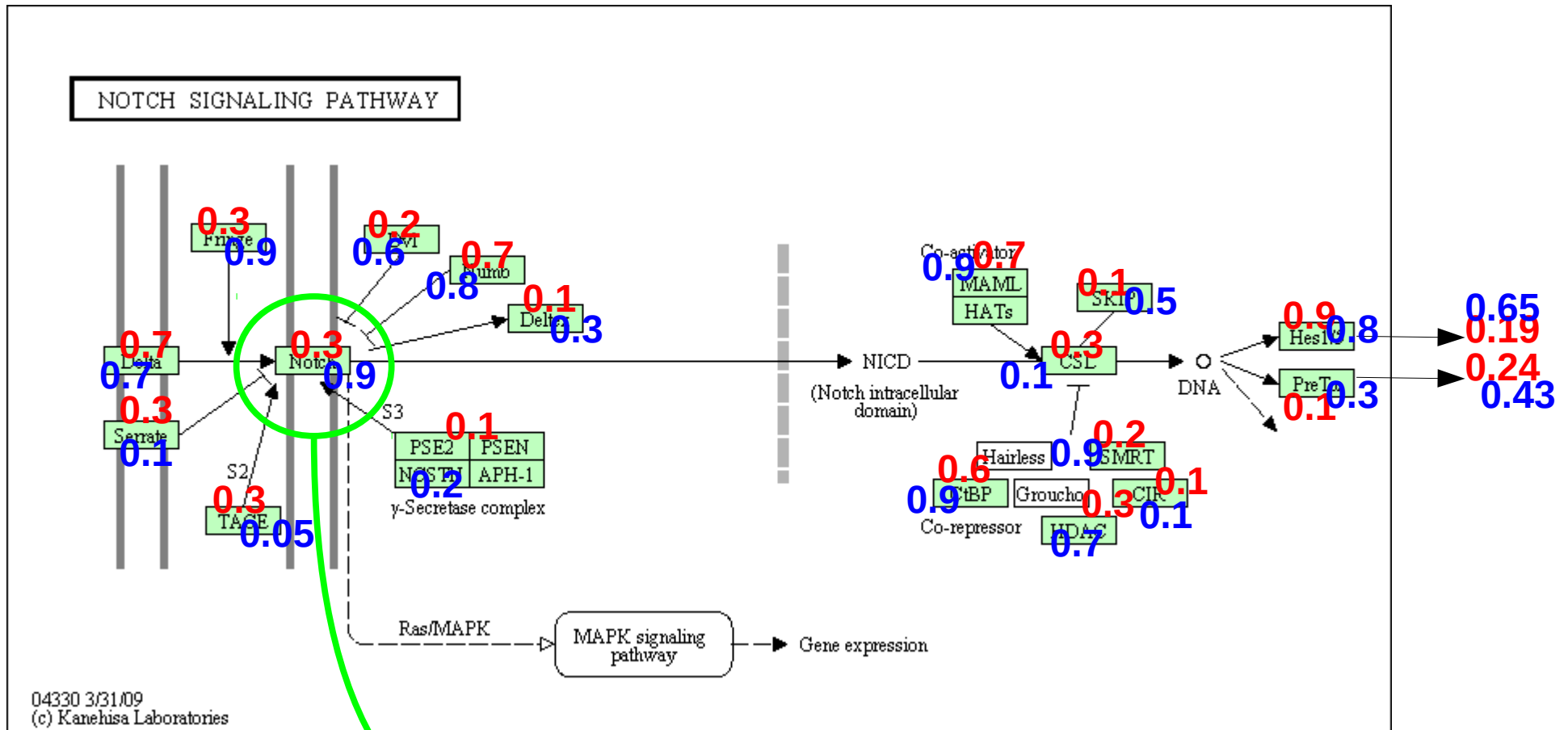
# Sequencing Data - First proposal



# Sequencing Data - First proposal



# Sequencing Data – Second proposal



$$P(\text{Functional}) = \epsilon \sum \text{freq}_{aa}$$

# Thank you!!!

