PathAct

In silico modulation of signal transduction

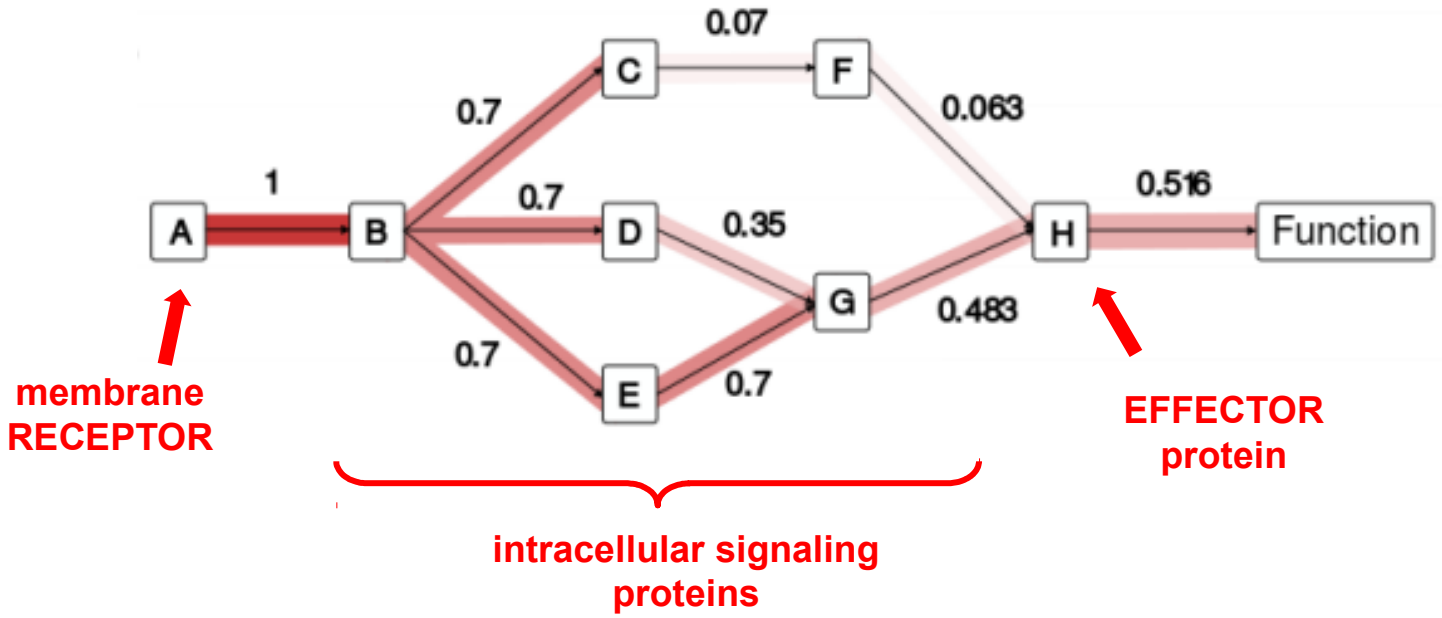
Marta R. Hidalgo

June 22th, 2018

PRINCIPE FELIPE
CENTRO DE INVESTIGACION

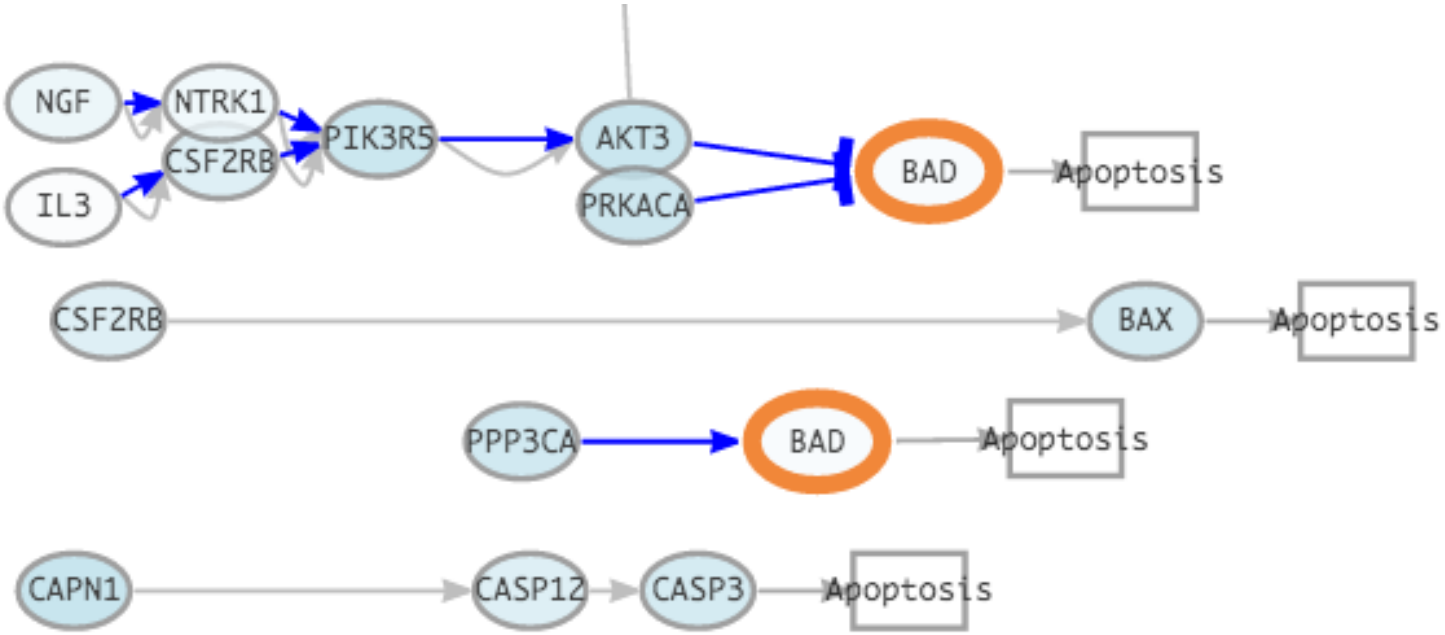
Signal transduction modelling

In our model, signal transduction is usually modulated through all nodes between a membrane receptor and an effector protein



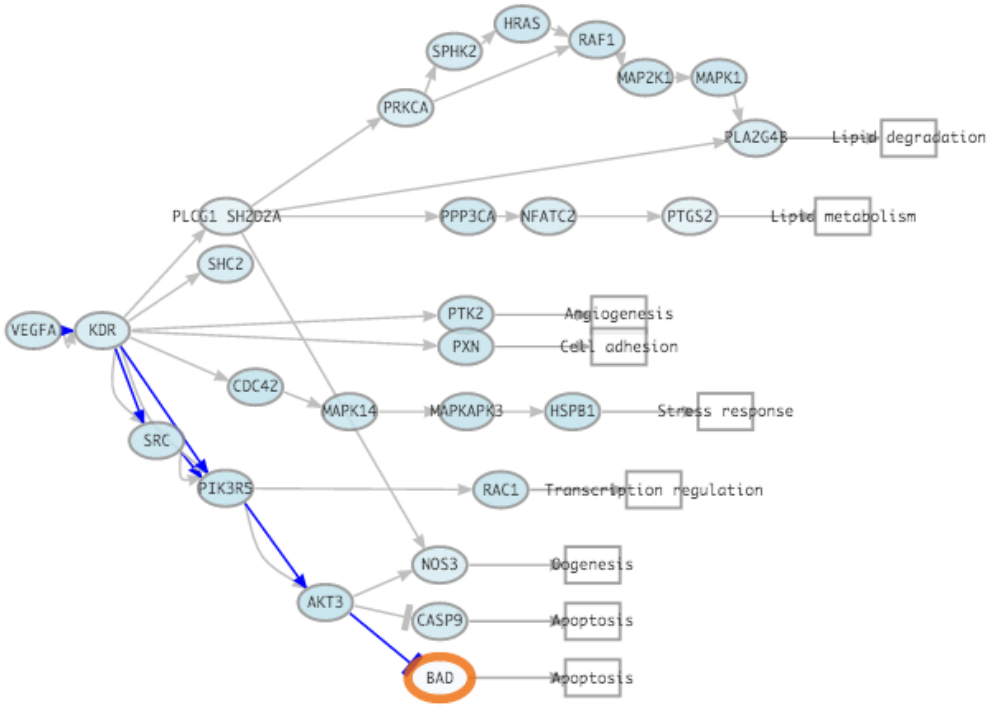
Signal transduction modelling

We can use the same machinery **to virtually explore the consequences of knocking out** (or overexpress) a gene in signal transduction.



Signal transduction modelling

This approach offers a powerful framework to design targeted therapies with minimum resources

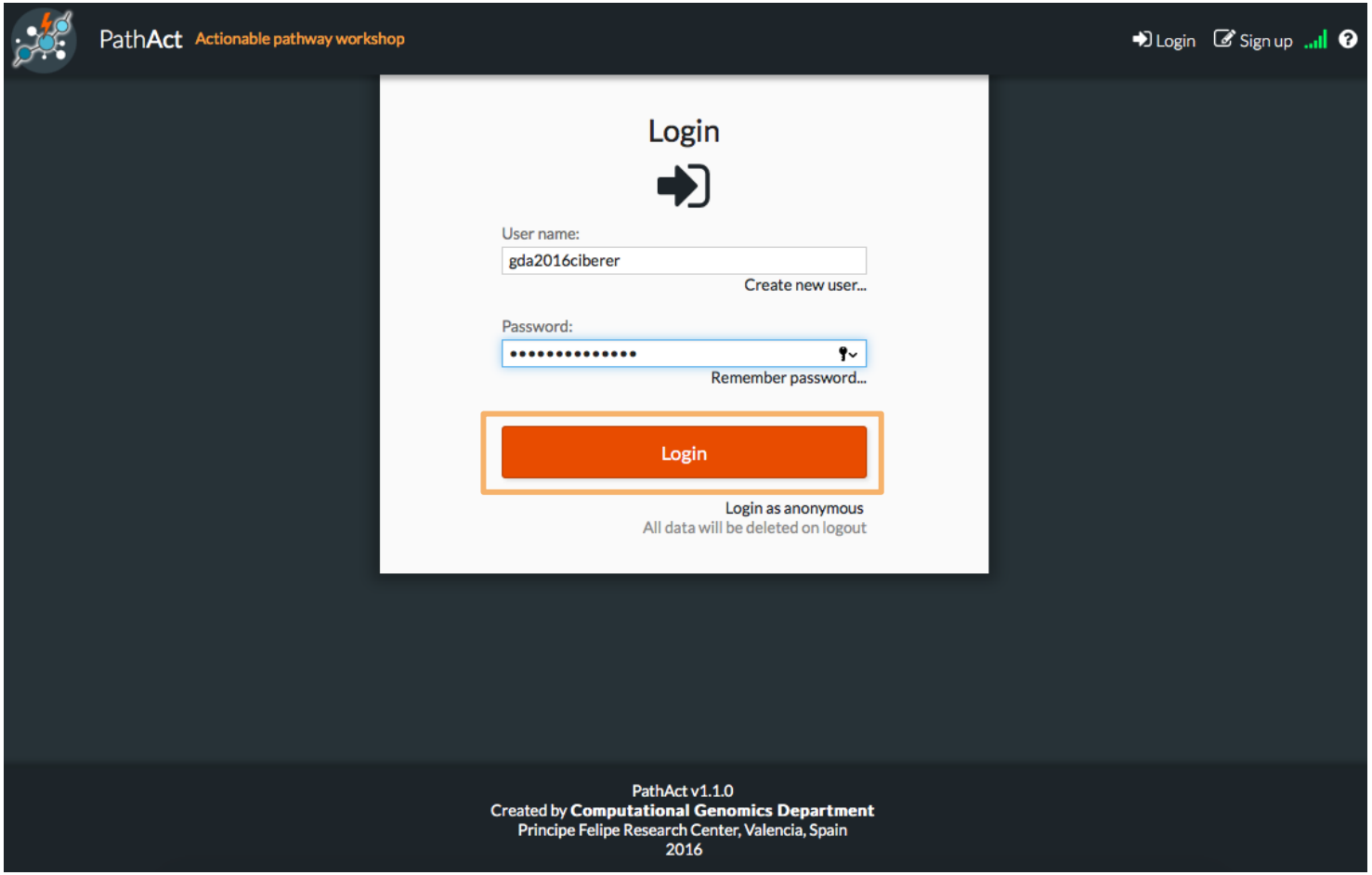


PathAct Web Tool

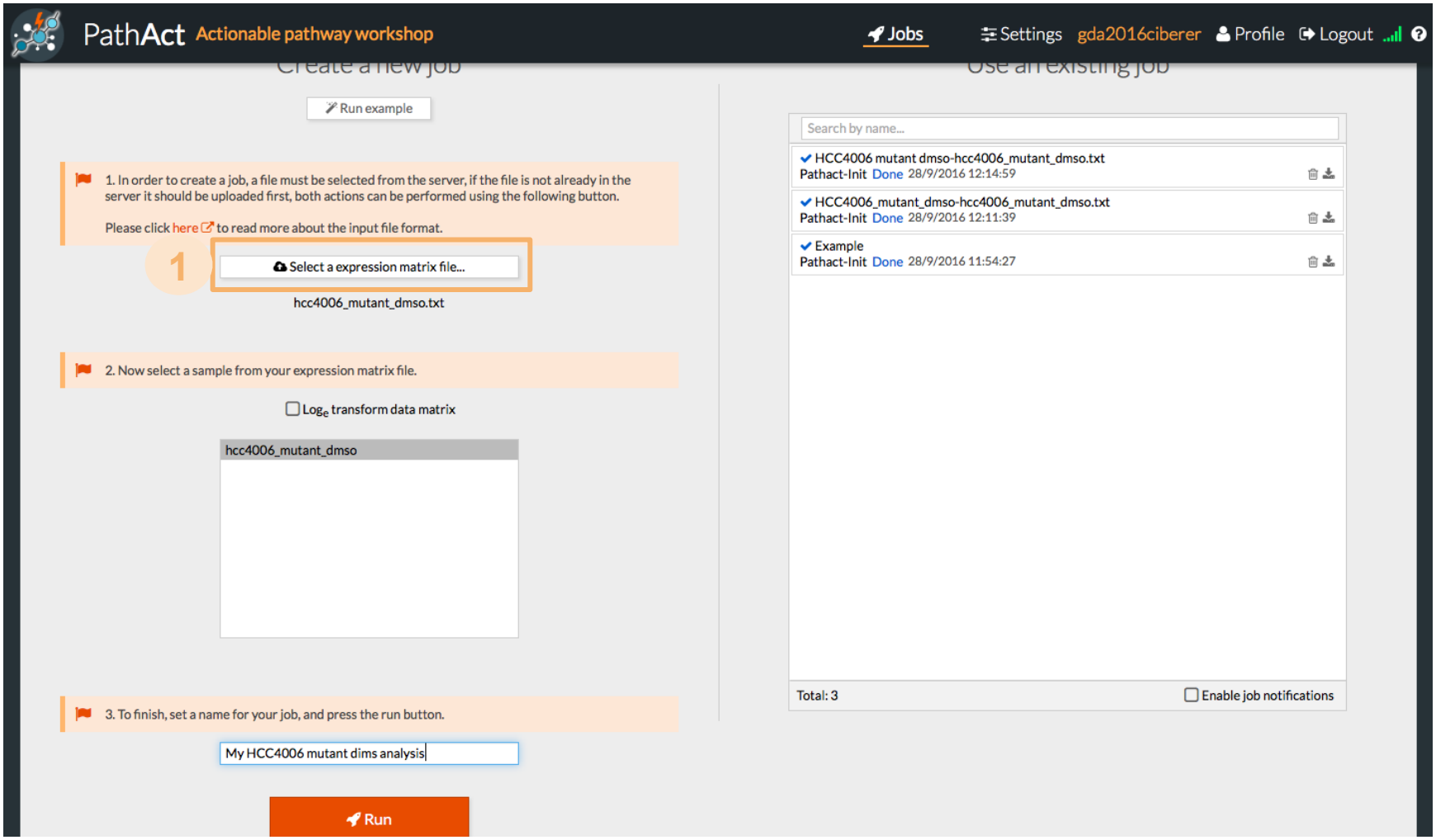
http://pathact-course.clinbioinfosspa.es/

PathAct Web Tool

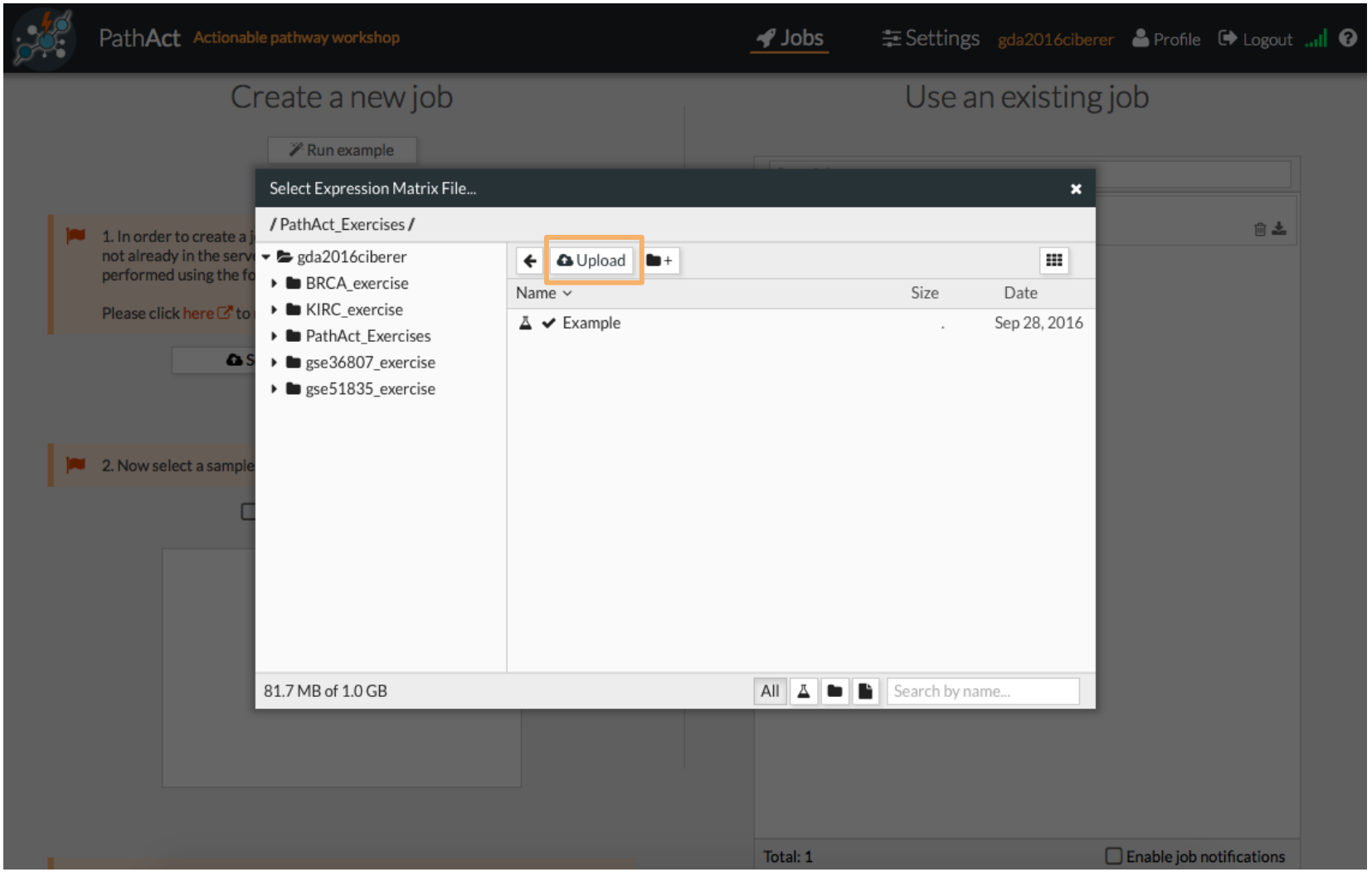
http://pathact-course.clinbioinfosspa.es/



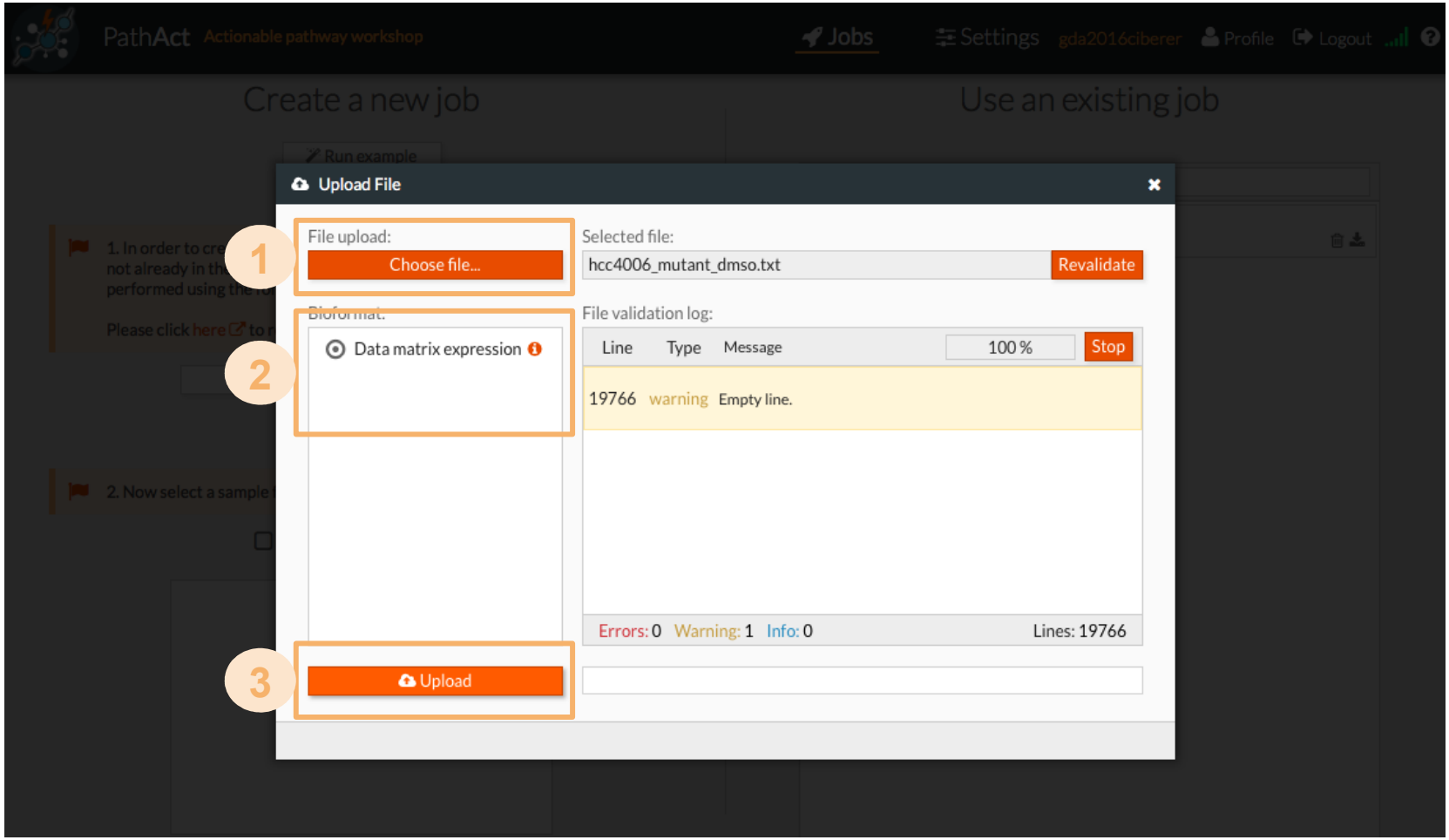
PathAct Web Tool



PathAct Web Tool



PathAct Web Tool



Select data

gene expression data
http://bioinfo.cipf.es/gda16ciberer

File format

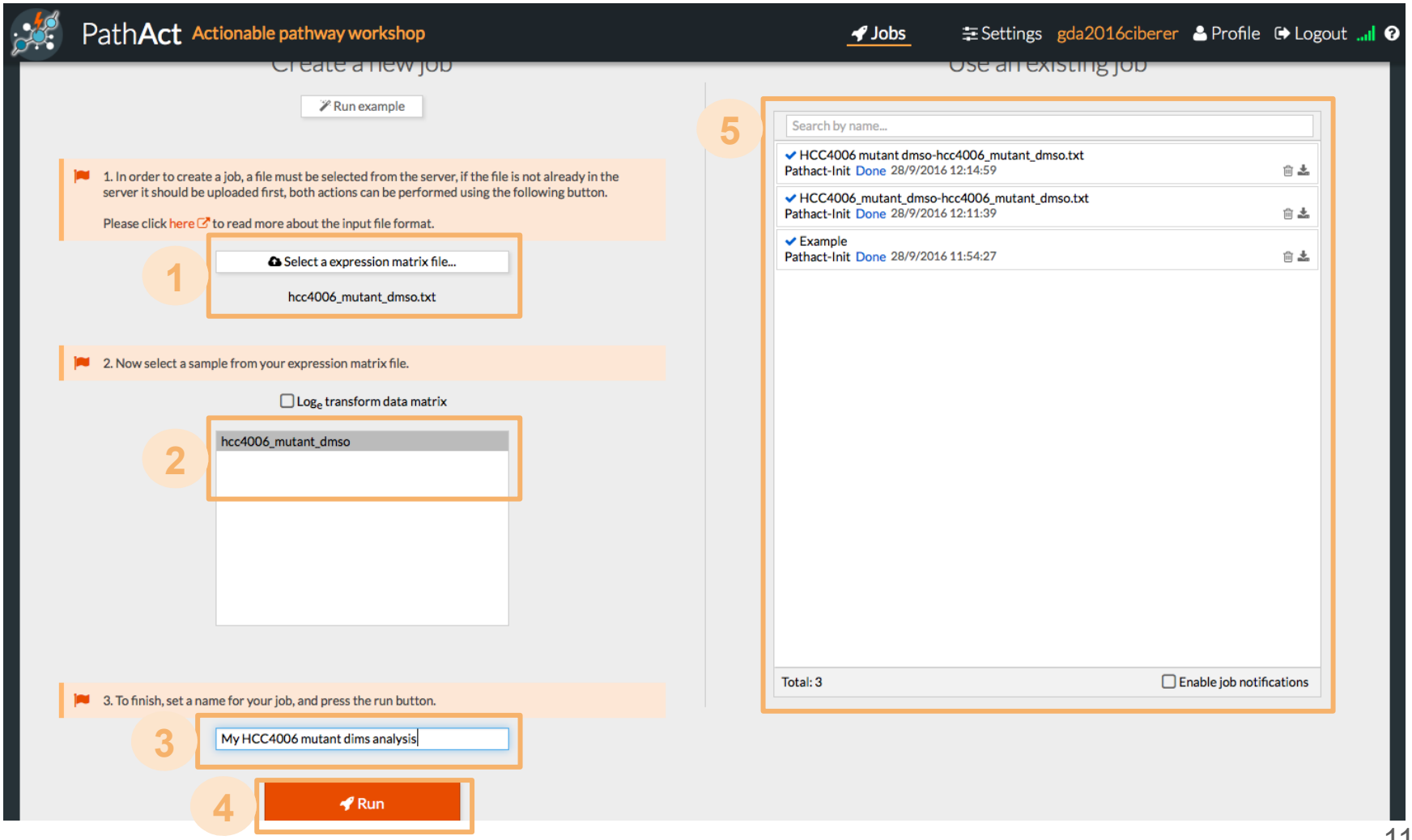
Columns: GeneIDs + Sample
Rows: EntrezGene (id)

Example

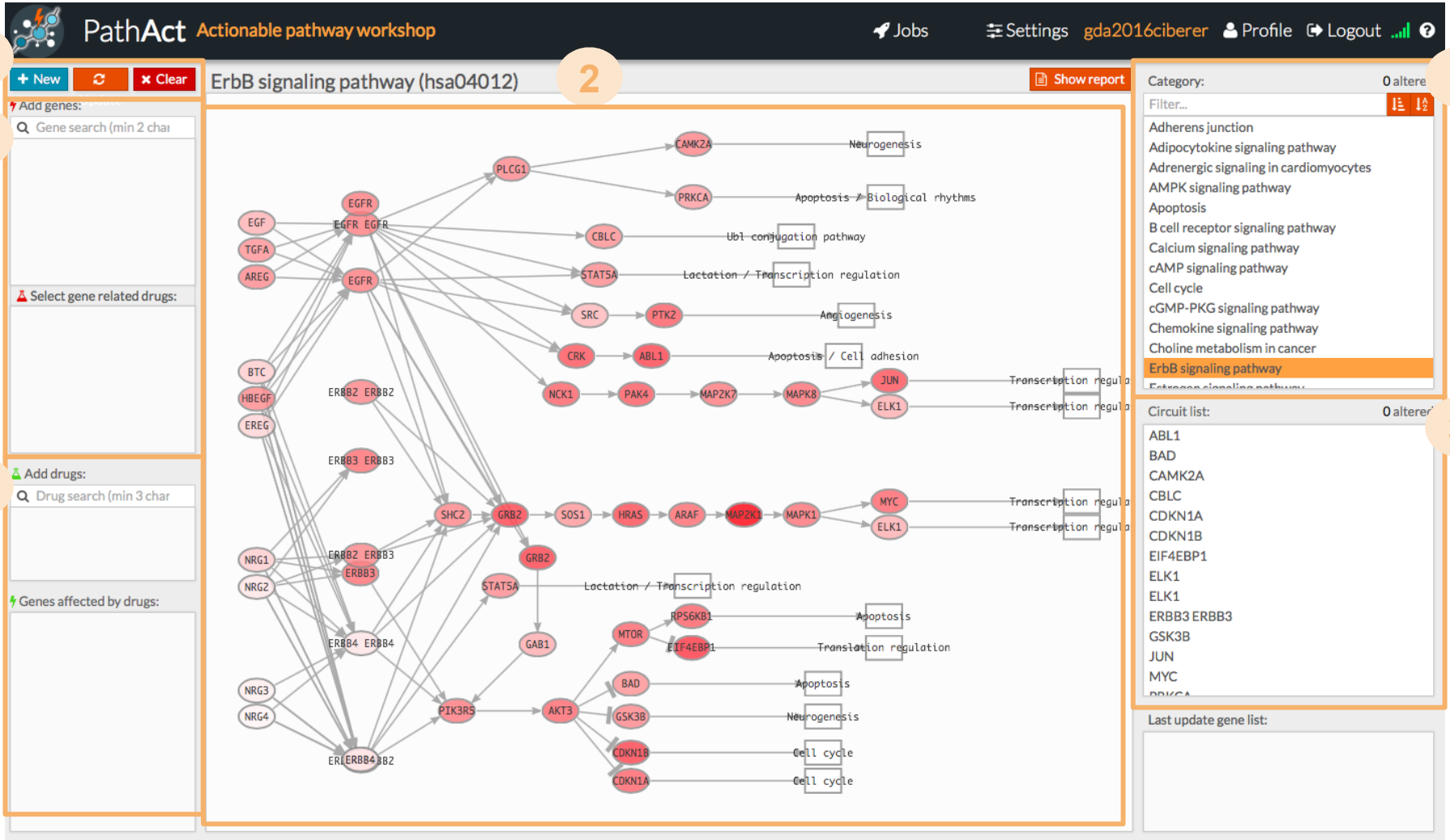
Non-small cell lung cancer (NSCLC)
EGFR mutant
Not treated with Erlotinib (TKIs)

geneID	hcc4006_mutant_dmso
1	5.99830927735415
10	4.26909388237212
100	7.90281107406193
1000	8.46383745767134
10000	5.82801370891263
100009676	5.95028396323201
10001	9.24054483957849
10002	4.50114481512442
10003	2.84739433259492
10004	4.59393709385877
100048912	3.2801596933055
10005	7.61874234203795
10006	8.67399667422145
10007	9.68407263257293
10008	4.72208873889579
10009	8.67753823201646
100093630	9.99164686804014
100093698	2.90650126505663
1001	11.4324736716045
10010	8.27543394593235
100101467	5.19948516713951
100101938	4.20778055144368
10011	9.43505129657583
100113407	3.3861342172626
100124700	4.55907367543182
100125288	5.92518975661431
100126784	5.23839965772242

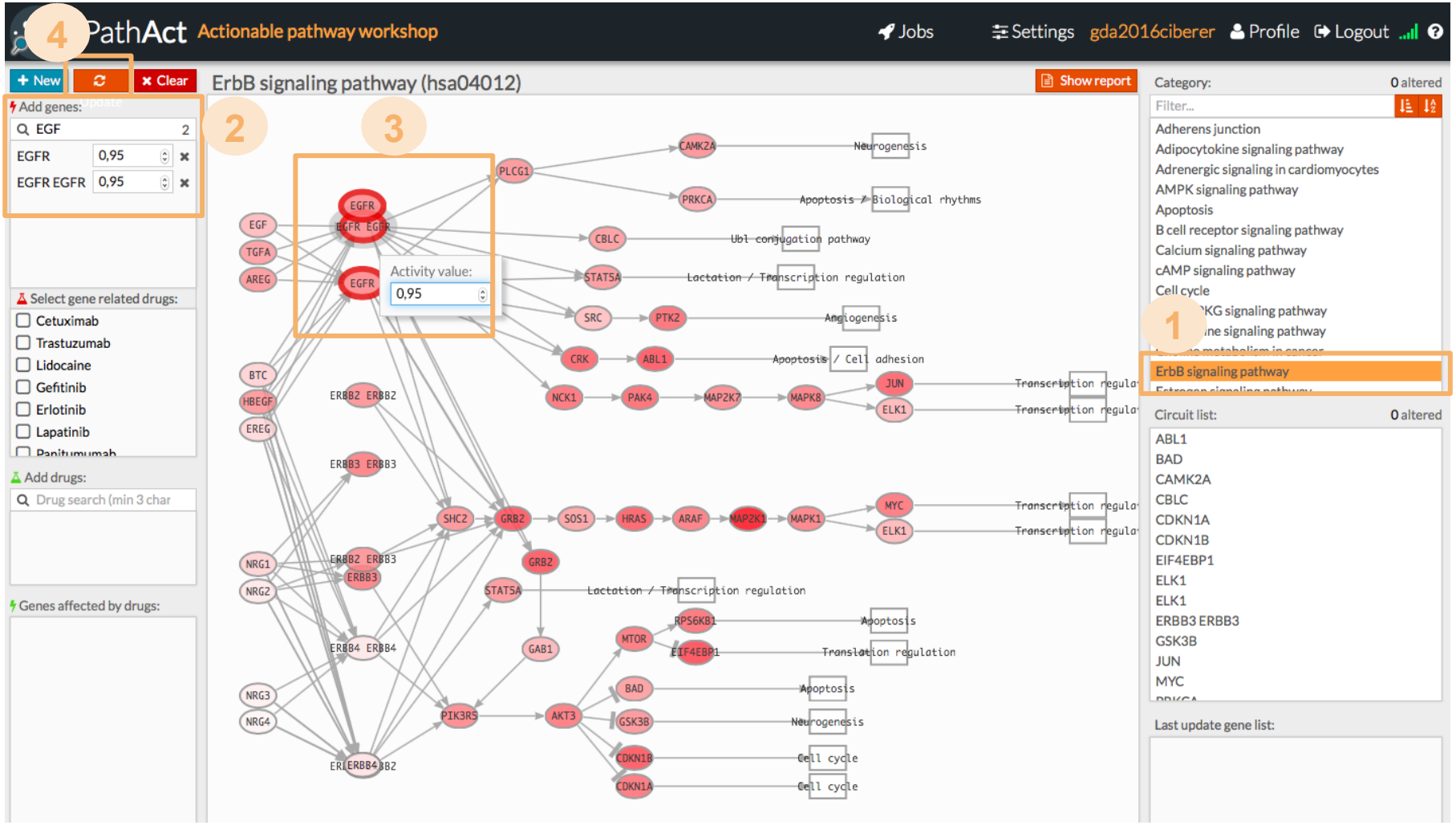
Select data


PathAct Actionable pathway workshop
Jobs
Settings
gda2016ciberer
Profile
Logout
Run example
1. In order to create a job, a file must be selected from the server, if the file is not already in the server it should be uploaded first, both actions can be performed using the following button.
Please click here to read more about the input file format.
1
Select a expression matrix file...
hcc4006_mutant_dmso.txt
2. Now select a sample from your expression matrix file.
Log$_e$ transform data matrix
2
hcc4006_mutant_dmso
3. To finish, set a name for your job, and press the run button.
3
My HCC4006 mutant dims analysis
4
Run
5
Search by name...
HCC4006 mutant dmso-hcc4006_mutant_dmso.txt
Pathact-Init Done 28/9/2016 12:14:59
HCC4006_mutant_dmso-hcc4006_mutant_dmso.txt
Pathact-Init Done 28/9/2016 12:11:39
Example
Pathact-Init Done 28/9/2016 11:54:27
Total: 3
Enable job notifications

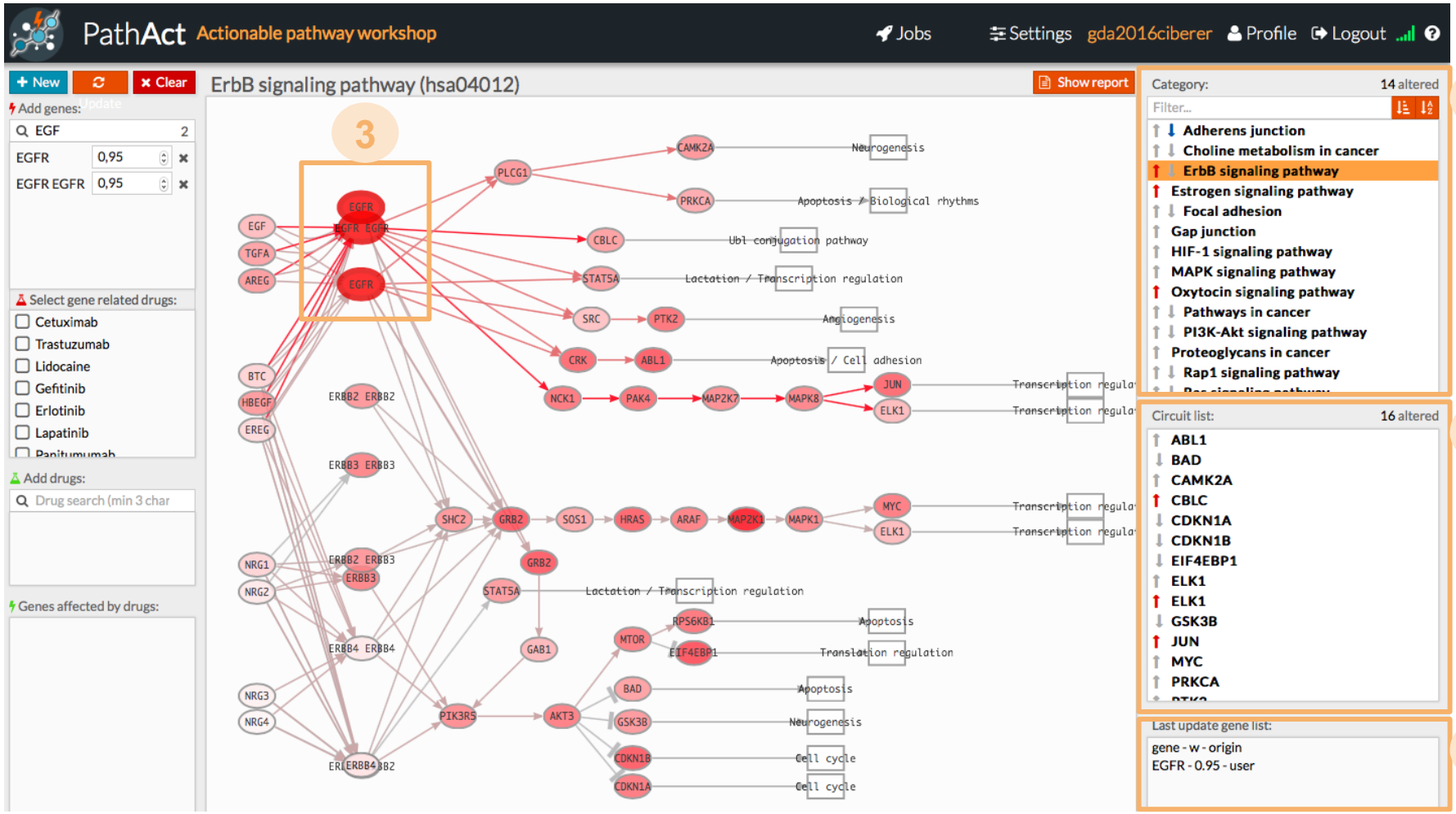
Overexpression



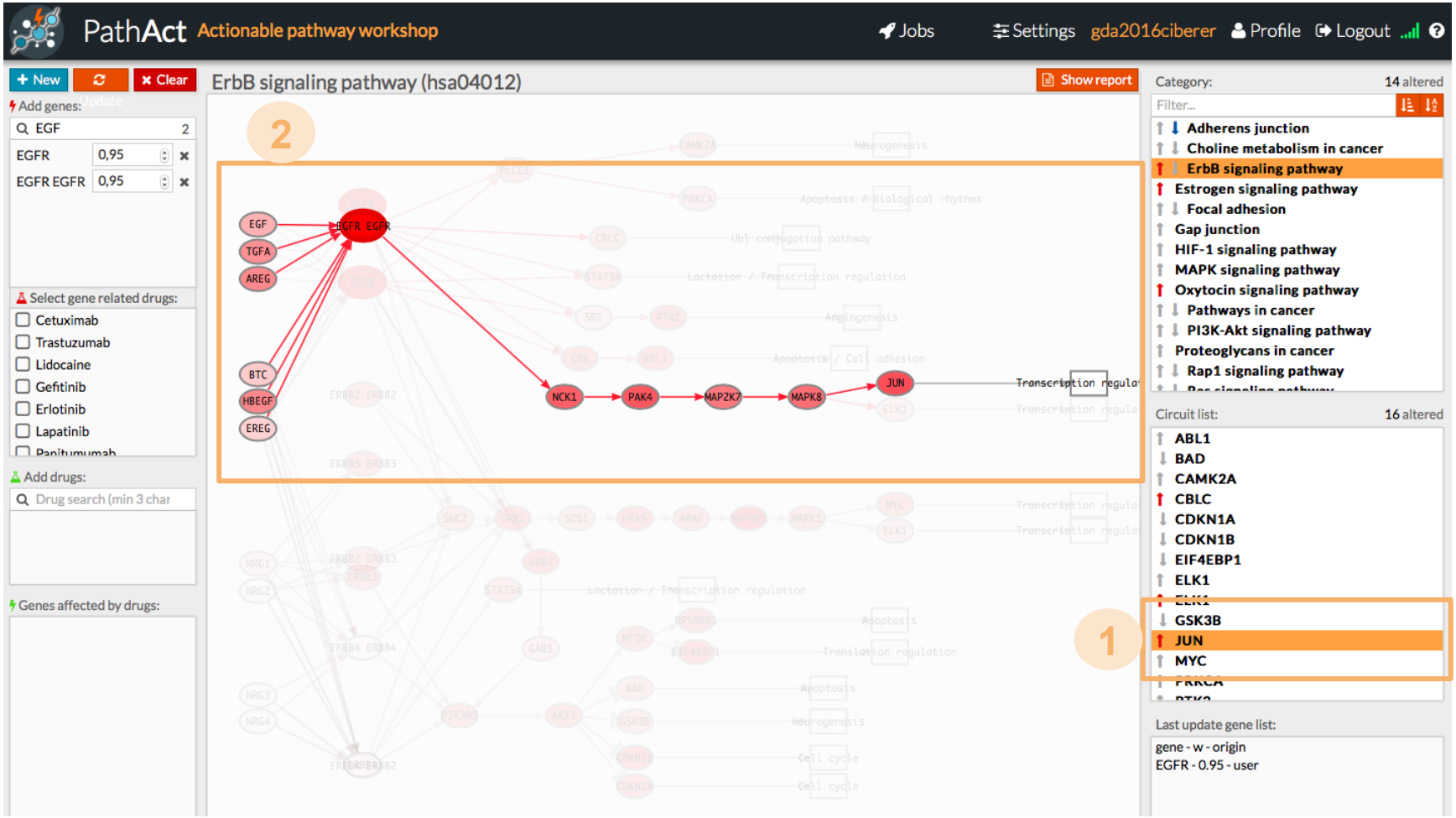
Overexpression



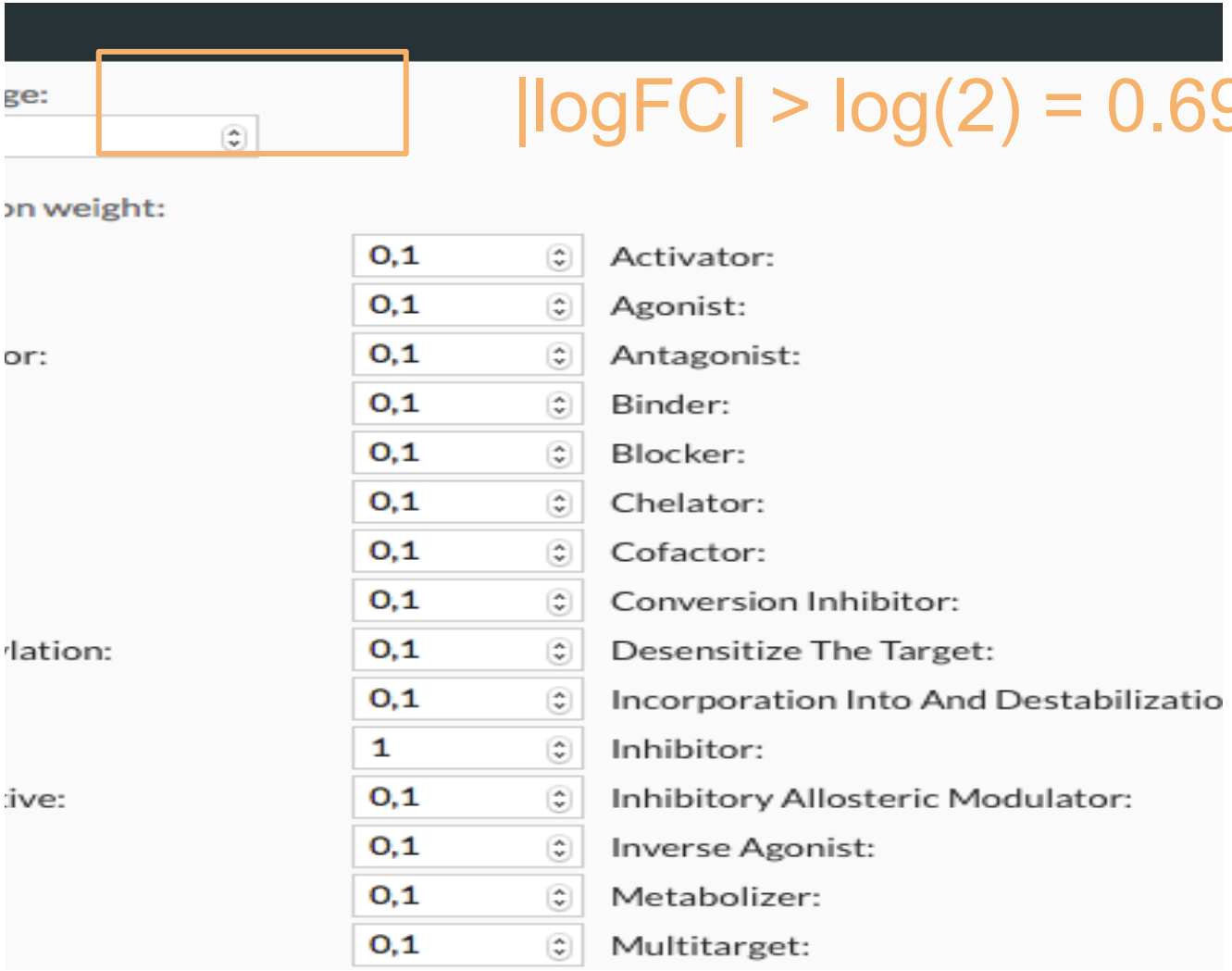
Overexpression



Overexpression

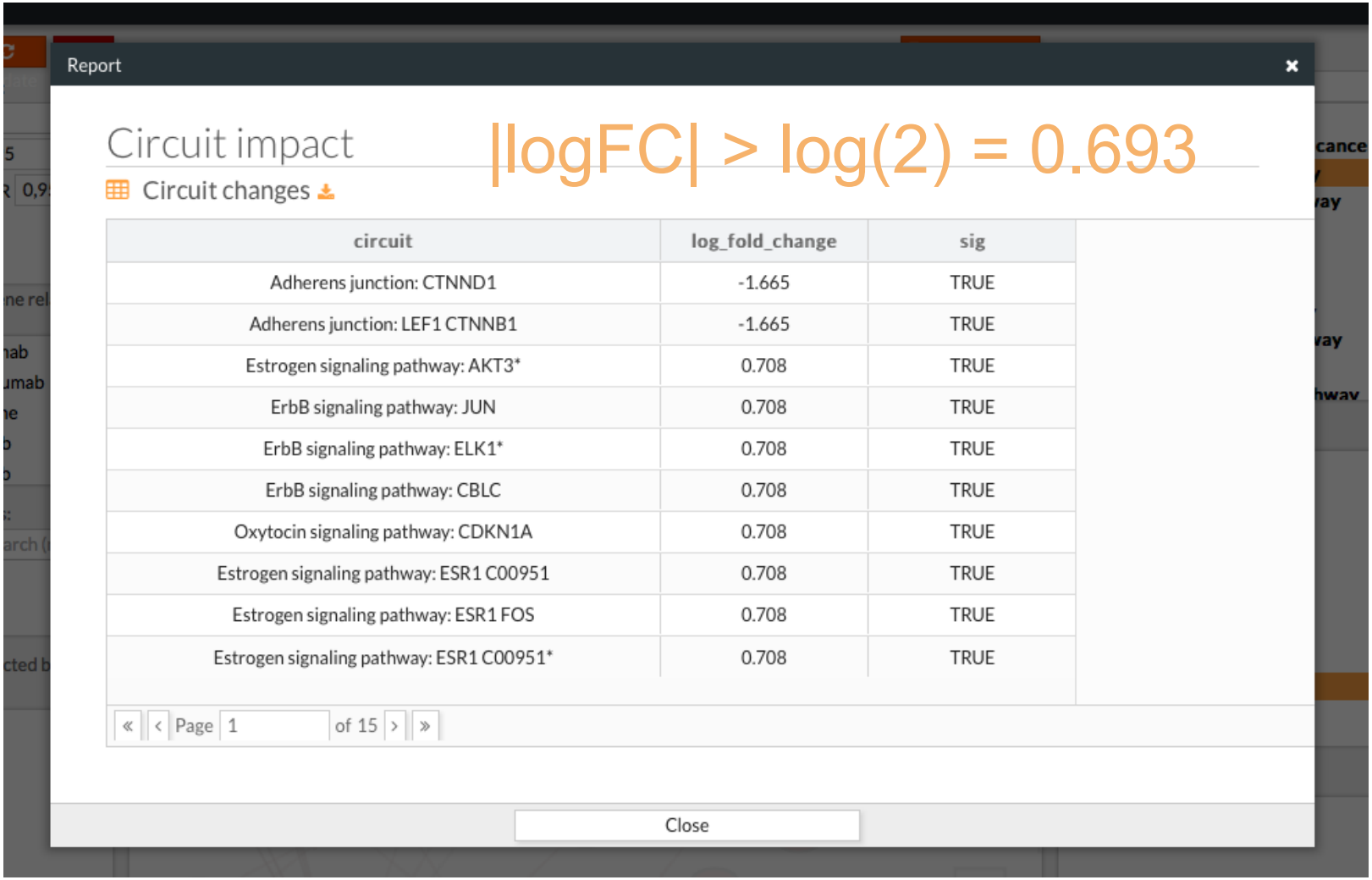


Results interpretation

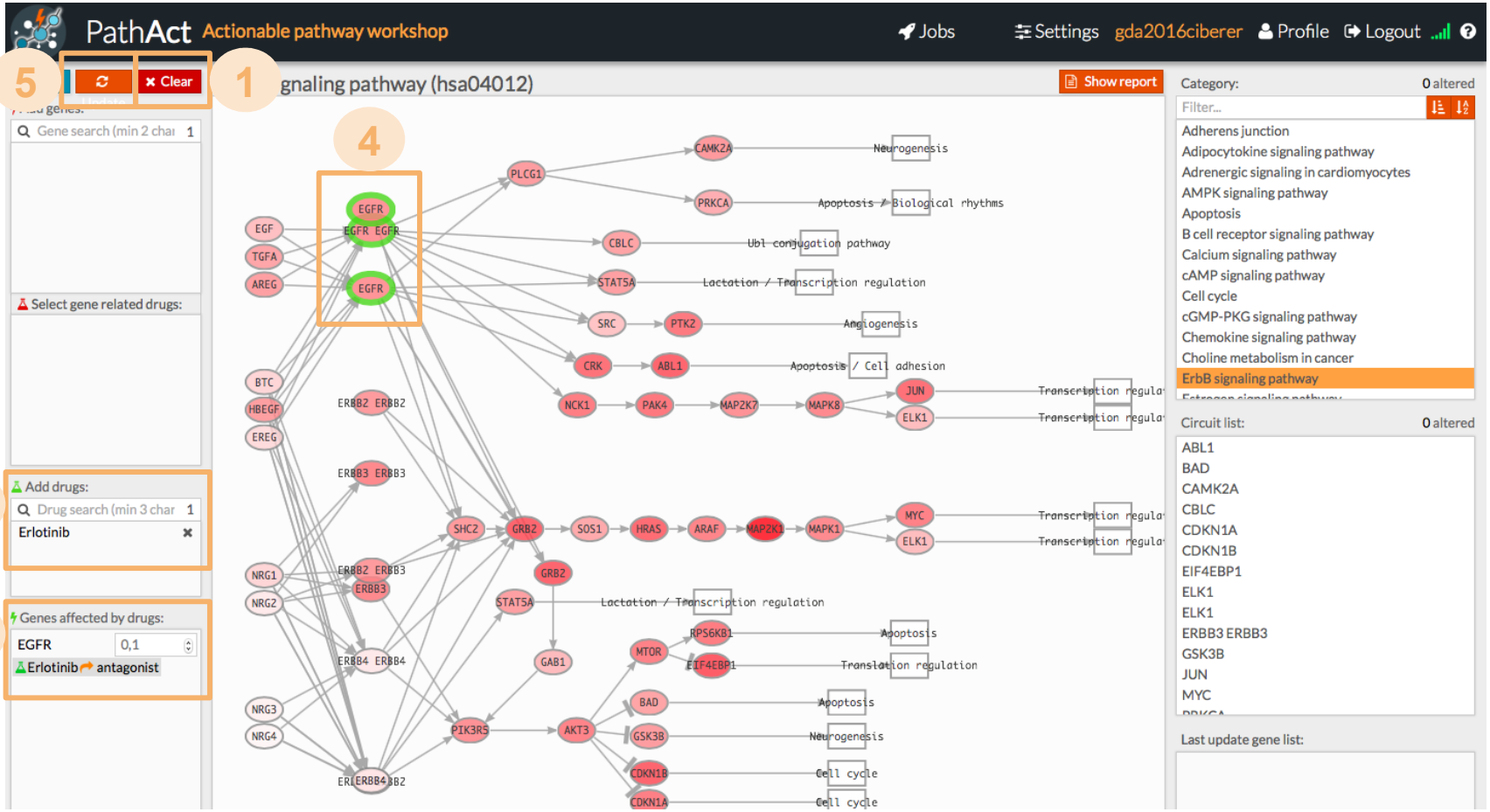


$|logFC| > log(2) = 0.693$

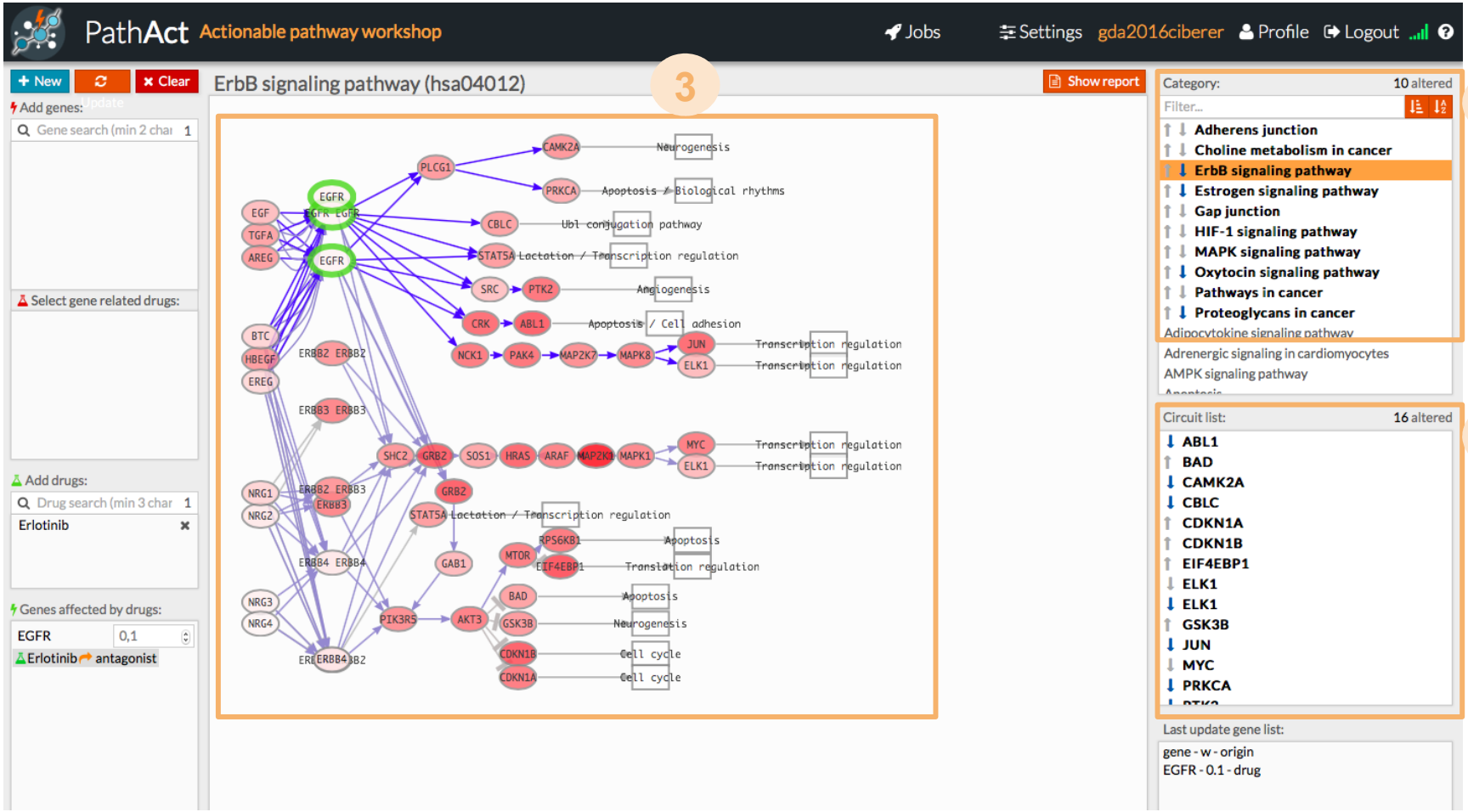
Report


Report
Circuit impact
|logFC| > log(2) = 0.693
Circuit changes
circuit
log_fold_change
sig
Adherens junction: CTNND1
-1.665
TRUE
Adherens junction: LEF1 CTNNB1
-1.665
TRUE
Estrogen signaling pathway: AKT3*
0.708
TRUE
ErbB signaling pathway: JUN
0.708
TRUE
ErbB signaling pathway: ELK1*
0.708
TRUE
ErbB signaling pathway: CBLC
0.708
TRUE
Oxytocin signaling pathway: CDKN1A
0.708
TRUE
Estrogen signaling pathway: ESR1 C00951
0.708
TRUE
Estrogen signaling pathway: ESR1 FOS
0.708
TRUE
Estrogen signaling pathway: ESR1 C00951*
0.708
TRUE
Page 1 of 15
Close

Drug action


PathAct
Actionable pathway workshop
Jobs
Settings
gda2016ciberer
Profile
Logout
5
Clear
1
gnaling pathway (hsa04012)
Show report
4
Gene search (min 2 char 1
Select gene related drugs:
2
Add drugs:
Drug search (min 3 char 1
Erlotinib
3
Genes affected by drugs:
EGFR
0,1
Erlotinib antagonist
Category:
0 altered
Filter...
Adherens junction
Adipocytokine signaling pathway
Adrenergic signaling in cardiomyocytes
AMPK signaling pathway
Apoptosis
B cell receptor signaling pathway
Calcium signaling pathway
cAMP signaling pathway
Cell cycle
cGMP-PKG signaling pathway
Chemokine signaling pathway
Choline metabolism in cancer
ErbB signaling pathway
Circuit list:
0 altered
ABL1
BAD
CAMK2A
CBLC
CDKN1A
CDKN1B
EIF4EBP1
ELK1
ELK1
ERBB3 ERBB3
GSK3B
JUN
MYC
Last update gene list:
EGF
TGFA
AREG
BTC
HBEGF
EREG
NRG1
NRG2
NRG3
NRG4
EGFR
EGFR EGFR
EGFR
ERBB2 ERBB2
ERBB3 ERBB3
ERBB2 ERBB3
ERBB3
ERBB4 ERBB4
ERBB4 ERBB2
PLCG1
CAMK2A
Neurogenesis
PRKCA
Apoptosis / Biological rhythms
CBLC
Ubl conjugation pathway
STAT5A
Lactation / Transcription regulation
SRC
PTK2
Angiogenesis
CRK
ABL1
Apoptosis / Cell adhesion
NCK1
PAK4
MAP2K7
MAPK8
JUN
ELK1
SHC2
GRB2
SOS1
HRAS
ARAF
MAP2K1
MAPK1
MYC
ELK1
GRB2
STAT5A
Lactation / Transcription regulation
GAB1
PIK3R5
AKT3
MTOR
RPS6KB1
Apoptosis
EIF4EBP1
Translation regulation
BAD
Apoptosis
GSK3B
Neurogenesis
CDKN1B
Cell cycle
CDKN1A
Cell cycle

Drug action


PathAct
Actionable pathway workshop
Jobs
Settings
gda2016ciberer
Profile
Logout
New
Clear
Add genes:
Update
Gene search (min 2 char
Select gene related drugs:
Add drugs:
Drug search (min 3 char
Erlotinib
Genes affected by drugs:
EGFR
0,1
Erlotinib antagonist
ErbB signaling pathway (hsa04012)
3
Show report
Category:
10 altered
Filter...
Adherens junction
Choline metabolism in cancer
ErbB signaling pathway
Estrogen signaling pathway
Gap junction
HIF-1 signaling pathway
MAPK signaling pathway
Oxytocin signaling pathway
Pathways in cancer
Proteoglycans in cancer
Adipocytokine signaling pathway
Adrenergic signaling in cardiomyocytes
AMPK signaling pathway
1
Circuit list:
16 altered
ABL1
BAD
CAMK2A
CBLC
CDKN1A
CDKN1B
EIF4EBP1
ELK1
ELK1
GSK3B
JUN
MYC
PRKCA
2
Last update gene list:
gene - w - origin
EGFR - 0.1 - drug
CAMK2A
Neurogenesis
PLCG1
PRKCA
Apoptosis / Biological rhythms
EGF
TGFA
AREG
EGFR
CBLC
Ubl conjugation pathway
STAT5A
Lactation / Transcription regulation
SRC
PTK2
Angiogenesis
CRK
ABL1
Apoptosis / Cell adhesion
BTC
HBEGF
EREG
NCK1
PAK4
MAP2K7
MAPK8
JUN
ELK1
Transcription regulation
ERBB2 ERBB2
ERBB3 ERBB3
SHC2
GRB2
SOS1
HRAS
ARAF
MAP2K1
MAPK1
MYC
NRG1
NRG2
ERBB2 ERBB3
GRB2
STAT5A
RPS6KB1
MTOR
EIF4EBP1
Apoptosis
Translation regulation
ERBB4 ERBB4
GAB1
NRG3
NRG4
PIK3R5
AKT3
BAD
GSK3B
Neurogenesis
CDKN1B
CDKN1A
Cell cycle

Thanks for your attention

Any questions?