

The **IPA Upstream Regulator Analytic** enables you to identify the cascade of upstream transcriptional regulators that can explain the observed gene expression changes in a dataset and illuminate the biological activities occurring in the tissues or cells being studied. IPA makes it easy to take this result even further by examining what biological processes, pathways, and diseases the transcriptional regulators and their targets may control, and how these upstream molecules may regulate one another's activities.

Feature Highlight
Upstream Regulator
& Downstream
Effects Analysis

Upstream Regulator Analysis in IPA is a remarkable step forward in the field of transcription regulator prediction. Unlike other tools, IPA will predict which transcriptional regulators are involved and whether they are likely activated or inhibited. IPA can then visualize this network of regulators and targets to explain how the regulators interact with one another and their targets to provide testable hypothesis for gene regulatory networks.

1

Step 1 – Run an analysis on your dataset: Select **File>New**, and select either **Core Analysis** or **Tox Analysis**

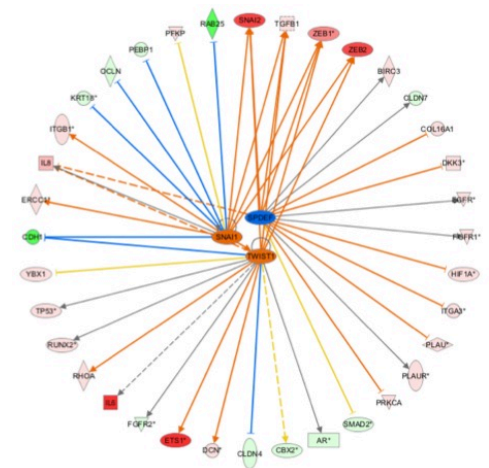
2

Step 2 – After the analysis completes, double-click the analysis name to open the Summary tab (default view).

3

Step 3 – Click the **Upstream Regulators** tab to see the upstream regulator results in the table view.

Upstream Regulator	Log Ratio	Molecule Type	Predicted Acti...	Activation z-score	p-value of overlap	Target molecu...
lipopolysaccharide		chemical drug	Activated	3.012	1.47E-06	Acot1, ...all 19
GnRH analog		biologic drug	Activated	2.630	2.06E-04	ACAA2, ...all 7
CEBPA		transcription regula	Activated	2.219	3.26E-04	APOA4, ...all 7
XBP1 (includes EG...		transcription regula	Activated	2.200	5.77E-04	ATP2A2, ...all 5
TNF		cytokine	Activated	2.648	6.30E-04	11000, ...all 14
CD28		other	Activated	2.236	1.14E-03	CFLAR, ...all 6
phorbol myristate a		chemical drug	Activated	2.179	1.87E-02	ATP2A2, ...all 8
HGF		growth factor	Activated	2.190	2.85E-02	CFLAR, ...all 5
OSM		cytokine	Activated	2.235	3.79E-02	ACAA1, ...all 5
pirinixic acid		chemical toxicant	Inhibited	-2.832	1.18E-19	ACAA1, ...all 22
PPARA		ligand-dependent	Inhibited	-3.374	7.84E-13	ACAA1, ...all 16
CFTR		ion channel	Inhibited	-2.157	6.67E-10	ACAA1, ...all 8
clofibrate		chemical drug	Inhibited	-2.613	5.87E-08	ACAA1, ...all 7
prostaglandin J2		chemical - endoge	Inhibited	-2.216	8.85E-08	Cald1, ...all 5
fenofibrate		chemical drug	Inhibited	-2.768	1.56E-06	ACAA1, ...all 8
KLF15		transcription regula	Inhibited	-2.000	9.81E-06	Acot1, ...all 4
bezafibrate		chemical drug	Inhibited	-2.200	1.84E-05	Acot1, ...all 5
POR		enzyme	Inhibited	-2.200	9.99E-14	Acot1, ...all 13



From here you can investigate predictions, display the results as a network and optionally configure the table view or export the Upstream Regulator data.


The **IPA Downstream Effects Analysis** predicts increases or decreases in downstream biological activities occurring in the tissues or cells being studied. Using the direction of change of the genes in your dataset, IPA computes the likely effect (increase or decrease) on diseases and cell biological processes such as cancer, apoptosis, and cell migration.

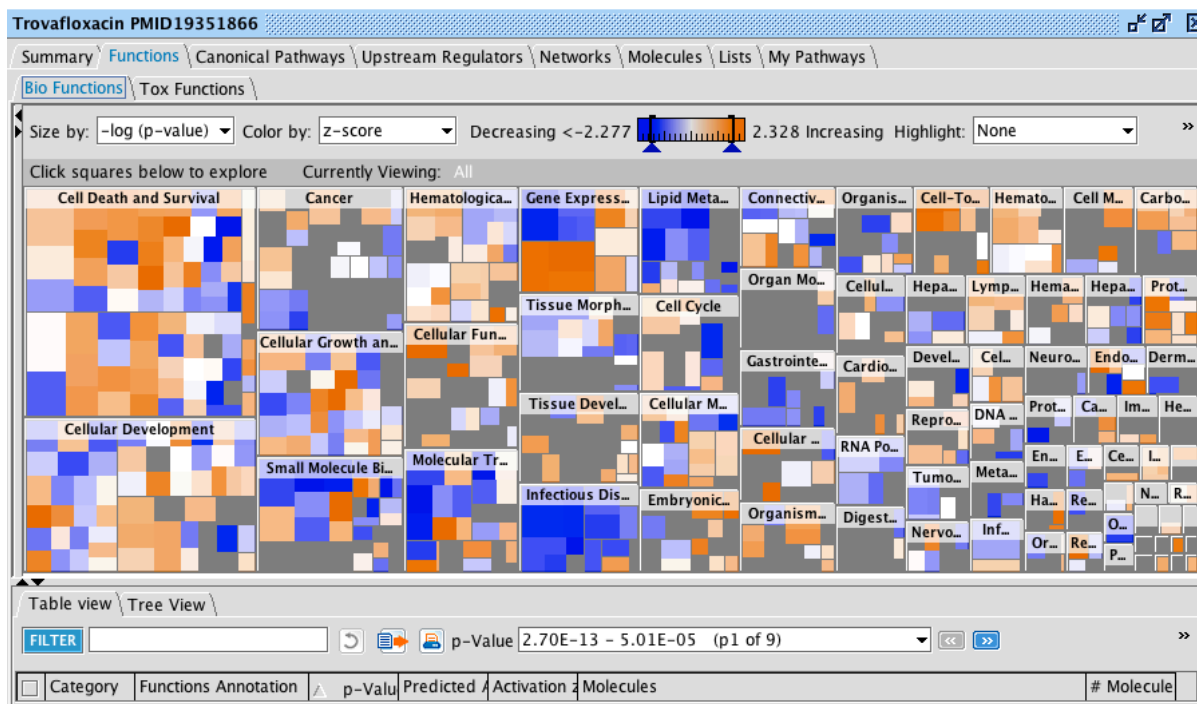
The Downstream Effects calculation underlies a new tool in IPA that enables the visualization of biological trends in an experiment in a whole new way. Other tools only indicate which biological processes might be affected, ignoring the actual direction of change of the genes that were measured. Downstream Effects Analysis takes you to faster insights by predicting whether there is an increase or decrease in the biological processes (functions) that interest you.

1

Step 1 – After running and opening analysis as described above, click the **Functions** tab to see the Downstream Effects Analysis results in the hierarchical heatmap and table view.

2

Step 2 – Click  (**Maximize**) in the upper-right corner to maximize the size of the Functions tab.



3

Step 3 – Review the data. Orange squares predict increases and blue squares predict decreases in the function or disease

4

Step 4 – CDCA7: Known to increase Cancer and is **Upregulated** in the dataset therefore predicted to increase the function

Drill down to areas of interest by clicking on the colored squares. After you click through to a single square, a window will appear that describes how each gene in your dataset contributes to the prediction.

Learn more: Learn about how IPA can help you understand your data at: <http://www.ingenuity.com/ipa>